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SUMMARY:

This review examines if exfoliated, virus infected animal skin cells could be an important source of infectious Foot and Mouth Disease Virus (FMDV) aerosols. Infectious material rafting on skin cell aerosols is an established means of transmitting other diseases. The evidence for a similar mechanism for FMDV is: (1) FMDV is trophic for animal skin and FMDV epidermis titers are high, even in macroscopically normal skin; (2) Qualitative FMDV skin aerosol emission estimates appear consistent with measured aerosol emission rates and are orders of magnitude larger than the minimum infectious dose; (3) The timing of infectious FMDV aerosol emissions is consistent with the timing of high FMDV skin concentrations; (4) Measured FMDV aerosol sizes are consistent with skin aerosols; and (5) FMDV stability in natural aerosols is consistent with that expected for skin aerosols. While these findings support the hypothesis, this review is insufficient, in and of itself, to prove the hypothesis and specific follow-on experiments are proposed. If this hypothesis validates, (a) new FMDV detection, management, and decontamination approaches could be developed and (b) the relevance of skin cells to the spread of viral disease may need to be reassessed as skin cells may protect viruses against otherwise adverse environmental conditions.

25

26 **Key phrases:** Epidermal Desquamation, Virus Excretion, Aerosol Emission, Airborne

27 Transmission, Epidemiology

28

29 **1. Introduction**

30 Foot and mouth disease (FMD) is a highly contagious viral disease capable of causing
31 widespread epidemics among livestock. It has a major economic impact when outbreaks
32 occur in countries previously free from disease. The Foot and Mouth Disease virus
33 (FMDV) is virulent and has multiple known routes of transmission. These include direct
34 contact (e.g. viral entry through mucous membranes, cuts or abrasions during animal-to-
35 animal contact); indirect contact (e.g. fomites); ingestion (e.g. contaminated feed), and
36 the respiratory or airborne pathway (e.g. the inhalation of infectious aerosols) [1]. The
37 airborne pathway is suspected to play a key role in some outbreaks by causing disease
38 "sparks" or disease spread to regions remote from a primary infection site [2,3]. If not
39 detected in a timely fashion, such sparks can lead to major outbreaks. For example, the
40 widespread dissemination of FMDV during the catastrophic 2001 UK outbreak was
41 thought to be due to the inadvertent transport of animals with unrecognized FMDV
42 infection from a Prestwick Farm to areas previously free of FMDV [4].

43

44 Like other viral diseases with an airborne transmission pathway, the source of infectious
45 FMDV aerosols is generally considered to be virus exhaled from the respiratory system
46 [1]. However while whole-animal FMDV infected aerosols have been extensively
47 characterized, a literature search identified only one study [5] that directly demonstrated
48 that the respiratory system was a source of airborne FMDV.[1] It is also noteworthy that
49 one study [6] measured significant emissions of infectious FMD aerosol when swine

[1] Other potential sources of infectious FMDV aerosols were not ruled out by this study nor by an earlier study [10] which reported more virus recovered from the noses of animal handlers examining the head relative to other handlers examining other body regions.

50 were placed in looseboxes *after being killed* when, presumably, all respiratory release of
51 virus had ceased.
52
53 This review examines the possibility that FMDV infected skin cells may be an additional
54 source of infectious FMD aerosols. Early researchers did previously raise the possibility
55 that airborne FMDV infected skin cells might be important in disease transmission
56 [6,7,8]; however, this possibility was never systematically investigated. In contrast,
57 *respiratory* mucosal epithelial cells are known to be a primary site of initial infection
58 (pharynx), a main virus amplification site (mouth), and the site of persistent infection in
59 carrier ruminants (pharynx) [1,9]. It is also known that FMDV is often found in oral-
60 pharyngeal fluids containing cellular material while samples without cellular material are
61 typically negative [1,9]. Collectively these observations suggest that FMDV infected,
62 respiratory mucosal epithelial cells shed into respiratory fluids may contribute to
63 respiratory emissions of FMDV aerosols.
64
65 Mammalian skin actively sheds a significant number of skin cells (10^6 to 10^8 per day) into
66 the environment [11,12,13] and skin cells have been observed to comprise a significant
67 fraction (1 to 10%) of measured indoor and outdoor[2] aerosols and indoor dust
68 [14,15,16,17]. Bacteria, yeast, fungi, and viruses are present on the surface of skin cells,
69 e.g. *Noble* [18] and references within. When these skin cells mature and naturally
70 exfoliate, the infectious material can become airborne (see *Supplemental Material:*
71 *Particle Suspension Mechanisms*), travel to new hosts, and cause infection when inhaled

[2] Measurements reported here were taken near human habitats. Skin cells may not contribute significantly to the total atmospheric aerosol burden at locations well-removed from human/animal habitation (e.g. remote ocean).

or deposited directly onto the skin of the new host [11,19,20,21,22,23]. This mechanism is believed to be a significant source of bacterial infection for surgical procedures and other nosocomial infections [11,19]. Transmission of viral disease via the inhalation of infectious skin cells is less well studied, but may be documented in at least one case (see *Supplemental Material: Other Viral Diseases*).

The purpose of the current study is to systematically review published data relevant to the hypothesis that skin cells could be a source of infectious FMDV aerosols. Estimates are provided for: (a) skin cell shedding rates; (b) FMD skin concentrations, and (c) the shedding rate of FMDV infected skin cells. In addition, the expected characteristics of an infectious FMDV skin cell aerosol source are placed in context with known experimental data. These include measurements of whole animal FMDV aerosol emissions in relation to timing, aerosol stability, aerosol size, and magnitude. Suggestions for future experiments are provided.

1. Estimating the Shedding Rate of FMDV Infected Skin Cells

1.1. Animal Skin Cell Shedding Rate

As part of the normal skin growth cycle, mammalian skin cells normally move progressively from basal cells (stratum basale) within the epidermal layer of the skin outward to the stratum corneum, where old skin cells then exfoliate into the environment. In adult humans, the most studied species with respect to airborne skin cell emissions, healthy skin typically sheds 1 cell layer per day. Exfoliated skin cells are typically shed as individual hexagonal plates, 25 μm on a side, and 0.1 to 0.5 μm thick [12,13]. Mature

95 skin cells (corneocytes) can become airborne by air moving across the skin surface [24]
96 (see also *Supplemental Material: Particle Suspension Mechanisms*); however emissions
97 over a short period of time can significantly increase with mechanical abrasion (e.g.
98 rubbing of clothes or body parts [25]), physical activity [26,27], and/or washing [28].
99 Exfoliated skin cells in settled dust may become re-aerosolized by human (animal)
100 activity [14,21,22] (see also *Supplemental Material: Particle Suspension Mechanisms*).
101 The median aerodynamic diameter[3] of human skin cells is approximately 14 μm. In fresh
102 [26,29] and environmentally processed [17] emissions, skin cells are observed at both
103 smaller and larger sizes – although the size distribution of aerosols derived from skin
104 cells is not precisely defined in the current literature.
105
106 Human skin bears many similarities to the skin of domestic animals that have been
107 documented to emit airborne FMDV (e.g. swine, cattle, and sheep) [30,31,32,33,34,35].
108 The similarities include general structure, skin cell size, and epidermial cell turnover
109 time. Based on these similarities, swine, cattle, and sheep can be expected to normally
110 shed one layer of skin cells per day. Considering an animal's skin surface area, a nominal
111 epidermis thickness of 100 μm,[4] and an assumed a skin density of 1 g/cm^3; the estimated
112 mass of epidermal material shed per day is 2 g for swine and sheep and 10 g for cattle.[5]

[3] Aerodynamic diameter is a measure of how the aerosol will behave in the atmosphere and does not necessarily equal the physical aerosol dimension(s). This study uniformly uses this metric to compare aerosols.

[4] Epidermal thickness is known to vary between the glabrous (e.g. snout) and haired regions with a lesser variation between animal species [36]. The value chosen here is more reflective of the haired regions where published epidermal thicknesses include: 60 μm in cattle [34] 30 to 100 μm and 70 to 140 μm in swine [31], and 50 μm in sheep [35]. The nominal value used in this study includes both the living and non-living portions of the epidermis. This value was chosen to allow direct comparison with skin/epidermis FMD concentration measurements (data on FMD concentrations in the stratum corneum are not available).

[5] Emission rates are scaled from human emission rates based on relative surface area. Surface areas of 0.7 m^2 (swine), 2.9 m^2 (cattle), and 0.8 m^2 (sheep) were calculated assuming a 30 kg swine, 200 kg cow, and 30

113

114 **1.2. Animal Skin FMDV Concentrations**

115 While not a typical site for the initial FMDV infection, the skin is a major viral
116 replication site in most animals studied [1,8,39,40,41,42,43]. **Table 1** (and *Supplemental*
117 *Material: Supplemental Data Table 1*) summarizes the available literature on swine,
118 cattle, and sheep FMDV skin concentrations for the day on which infectious FMDV skin
119 concentrations are highest.[6] Infectious FMDV concentrations in skin on the body surface
120 are presented for both clinically abnormal external (non-oral) skin lesion material
121 (typically foot lesions) and in macroscopically normal (but infected) skin. As FMDV skin
122 concentrations are known to vary by body region, measurement data is presented for both
123 the trunk and extremity measurements.

124

125 FMDV is well known to be present in the macroscopic skin lesions characteristic of
126 clinically active disease. The rupture of these macroscopic skin lesions, with the
127 subsequent release of FMDV infected cell cytoplasm onto the surface of the skin
128 followed by exfoliation of the infected skin cells, is one pathway whereby FMDV could
129 become aerosolized,[7] i.e. FMDV "rafting" on outside of airborne skin cells [41,47,48].

130

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kg sheep using the methods described in [37,38]. Animal sizes were chosen to reflect animals used in FMD aerosol emission studies. For context, the adult human body surface area is 1.75 m^2 [29].

[6] Peak skin concentrations are typically co-incident (or at most within a single 24 hr sampling period) of the development of widespread visible (macroscopic) lesions, typically a few days after the initial infection [39,41,43,44]. FMDV levels in live animal skin tissues significantly decrease after antibodies begin to circulate a few days later. FMDV RNA (but not infectious FMD) has been reported in skin up to several weeks after infection [1,44,45,46].

[7] Presumably external contamination of the skin could also occur with other FMD-laden excretions. As summarized by *Alexandersen et al.* [1] many body excretions such as oral saliva, nasal secretions, urine, and feces contain infectious FMDV.

There is also the possibility that FMDV infected skin cells from clinically normal appearing skin could be a source for FMDV aerosol and disease transmission. All seven antigenic types of FMDV have been observed in the normal skin of infected animals (i.e. skin without clinically obvious, macroscopic lesions), albeit at a lower concentration than in lesional material. *Brown et al.* [41], *Brown et al.* [49], and *Guilinunas* [43] observed microscopic lesions to be present just below the stratum corneum in some (but not all) of the FMDV positive, clinically normal skin samples that were examined.

Within the skin itself, FMDV concentrations are highest (by several orders of magnitude) within the epidermis [41,43]. In-situ hybridization and immunofluorescence studies indicate that the initial FMDV replication site is located in the deeper basal layers of the epidermis (basal cells proper or the stratum spinosum layer just above) and that FMDV laden cells migrate outward towards the skin surface. There is no evidence of active virus replication in the stratum corneum [41,47,48,49]. *Brown et al.* [41] reported FMDV present within the cell cytoplasm of all epidermal skin layers in macroscopically normal epidermis. Other studies [47,49] have not observed FMDV signal in the intact, non-lesional, stratum corneum. There are no known studies of the infectivity of the stratum corneum in animal skin.

1.3. Peak FMDV Infected Skin Cell Shedding Rates

The peak FMDV skin cell shedding rate is estimated by multiplying the skin cell shedding rate by the peak FMDV skin concentrations (see the *Animal Skin Cell Shedding Rate* and *Peak Animal Skin FMDV Concentration* sections). This calculation yields a

peak FMDV skin cell shedding rate of approximately 10^6 $TCID_{50}$/animal/day for swine and cattle, respectively based on non-lesional FMDV skin concentration measurements.[8] This estimate is approximate and does not include the contributions of infected FMDV skin cells derived from lesional material - which contains orders of magnitude higher FMDV concentration than non-lesional skin. It also does not include the contribution of skin externally contaminated with infectious FMDV. Both of these mechanisms would be expected to increase the net infectious skin cell shedding rate. The fraction of shed skin cells that are aerosolized, either initially or at a later time, is likewise unknown, but the FMDV infected skin cell aerosol emission rate would be less than the skin cell shed rate estimated in this section. This estimate does not assume that all shed skin cells contain the same amount of infectious FMDV.

For perspective, it is informative to note that a recent review of the FMD infectious dose via the aerosol route suggested that the minimum FMD infectious dose is 11 $TCID_{50}$ for sheep, 25 $TCID_{50}$ for cattle, and 180 $TCID_{50}$ for swine [50]. The estimated peak FMDV skin cell emission rate of approximately 10^6 $TCID_{50}$/animal/day for swine and cattle exceeds these figures by orders of magnitude so in theory, FMDV could be transmitted via an infected skin cell pathway.[9] This daily FMD excretion rate from exfoliated skin cells is approximately the same magnitude as that estimated to be due to urine or feces [1]. It is also about 10 to 100 times greater than the FMD aerosol emissions measured directly from infected swine respiratory systems [5]. There are, however, important

[8] There is insufficient data on sheep skin concentrations to justify an emissions estimate.
[9] There is no data on the degree to which infectious FMDV could be released from the airborne skin cells that deposit within the respiratory system.

175 unknowns in the latter comparison. For example, the latter study did not account for
176 aerosol losses and so likely underestimated the total respiratory emissions.
177

178 **2. Providing Context to the Hypothesized FMD Skin Aerosol Source**

179 **2.1. Timing of FMDV Aerosol Emissions**

180 The timing of FMDV emergence in skin tissue is consistent with the skin being a source
181 of infectious aerosols. In swine (but less clearly in cattle and sheep), emissions of
182 airborne virus are observed to begin (and peak) co-incident with the onset of clinical
183 signs of FMD (e.g. the development of visible lesions outside the inoculation site) – the
184 time when FMDV skin concentrations peak. Emissions then persist for several days
185 [1,5,7,51,52]. While this may generally be the case, on occasion, airborne FMD has been
186 observed to begin on the day before clinical signs appear or alternately to begin as much
187 as several days after the development of clinically evident lesions. However, a general
188 association of FMDV aerosol emissions with clinical skin lesion development is
189 particularly strong in the swine experiments in which infection occurred via airborne or
190 direct contact.[10] In these experiments, most animals emitted no airborne virus prior to
191 skin lesion development and no airborne emissions were reported more than one day
192 prior to the development of the clinical signs of FMD [5,7,53].
193

194 **2.2. Whole Animal FMDV Aerosol Emission Rates**

195 While FMD was first proved to be capable of airborne spread in the 1930's [54], it was
196 not until the 1960's that detailed experiments were first performed to characterize the

[10] Other infection routes, e.g. inoculation in a foot, and the high dose exposure regimen typically used accelerate the rate of disease progression often yielded clinically evident lesions in the first 24 hr (smaller than the sampling timescale).

emission of infectious FMD aerosols. Many of the published laboratory studies of FMD aerosol emissions were performed at the UK Institute of Animal Health and have often been performed using similar experimental conditions. While it is beyond the scope of this study to provide a detailed review of the kinetics and magnitude of FMD aerosol emissions, **Table 2** (and *Supplemental Material: Supplemental Data Table 2*) provides a summary of published estimates of the peak whole-animal FMD aerosol emission rate – i.e. the average emission rate per animal per 24 hour period[11] for the day of maximum emissions.[12] The total amount of FMDV collected by the air sampler was converted into a 24 hour emission rate using Equation (1)[13] – using airborne FMDV concentrations either directly reported or calculated from Equation (2). Equation (1) was derived assuming a steady state air concentration (i.e. losses within the animal holding area are balanced by animal emissions), well-mixed air (i.e. air concentrations are the same at all locations within the loosebox), and a 4 m x 3 m x 3 m (3.6×10^4 L) loosebox.

$$\mathrm{FMDV}_{\mathrm{Emissions}} = \left[\mathrm{FDMV}\right]_{air} \times V_{loosebox} \times \left(L_{aerosol} + L_{ACH}\right) / \#_{\mathrm{Infected\,animals}} \qquad \text{Eq. (1)}$$

where

$\mathrm{FMDV}_{\mathrm{emissions}}$ = the FMDV aerosol emission rate in TCID_{50} per animal per day

[11] The reported values are normalized. The sampling period ranged from 5 minutes to 1 hour.
[12] The data reported corresponds to loosebox experiments in performed at UK Institute of Animal Health and assume similar aerosol loss rates. Additional data is available for a small (610 L) sampling chamber. However aerosol loss rates in this chamber have not been reported in the published literature and so Equations (1) or (2) cannot be used.
[13] This equation differs from that previously used in the literature [52], but incorporates new effects such as the FMDV aerosol loss rate and the size of the loosebox. The values reported here are broadly consistent with, although higher than, those previously reported.

$[FMDV]_{air}$ = the measured FMDV air concentration in $TCID_{50}$ per liter

$V_{loosebox}$ = loosebox volume ($3.6x10^4$ liters)

$L_{aerosol}$ = measured loosebox FMDV aerosol loss rate with no air exchange (144 / day)

(see the *FMDV Stability in Detached Skin and Whole Animal Aerosols* section)

L_{ACH} = air exchange rate during the sampling period

$\#_{Infected\ animals}$ = number of infected (FMDV excreting) animals in the loosebox

$$[\mathrm{FDMV}]_{air} = \frac{TotalFMDVCollected}{AirFlowRate \times t_{sampling}} \qquad \text{Eq. (2)}$$

where

TotalFMDVCollected = total amount of FMDV in the liquid sampling media in $TCID_{50}$

AirFlowRate = sampling instrument air flow rate in liters per minute

$t_{sampling}$ = sampling duration in minutes

Overall, the average per animal peak FMDV aerosol emission rate is estimated to be approximately 10^7 $TCID_{50}$ per day for swine and $10^{4.5}$ $TCID_{50}$ per day for cattle and sheep. These whole animal emission values are similar in magnitude to the infected skin cell shedding rate of 10^6 $TCID_{50}$ per day previously estimated for swine and cattle. One study compared whole animal (swine) infectious aerosol emission rates from live and dead animals and reported that FMDV aerosol concentrations (and thus emission rate) decreased by 10x to 100x when animals were slaughtered [6]. The dead swine FMDV aerosol emission rate was similar to that reported above for (live) sheep and cattle and is

239 10% of the total infected FMD skin cell shed rate estimated in the *Peak FMDV Infected*
240 *Skin Cell Shedding Rates* section.
241
242 **2.3. FMDV Stability in Detached Skin and Whole Animal Aerosols**
243 While there are no studies examining the stability of FMDV in skin aerosols, there are a
244 few studies that have examined FMDV stability in skin separated from live animals (i.e.
245 skin not subject to *in-vivo* antibody clearance). The available data suggests that the
246 FMDV lifetime in detached skin is long – from days to months. *Sellers et al.* [6]
247 demonstrated that FMDV concentrations in swine foot lesions did not decrease over a
248 24hr period. *Gailiunas and Cottral* [55] demonstrated that FMDV in clinically normal
249 bovine hides consistently remained infectious (and virulent) for weeks to months in
250 storage. These samples were either dried (20ºC, 40% humidity) or salt/brine-cured
251 (temperatures ranged from 4ºC to 15ºC and humidity ranged from 40% to 90%).
252
253 The two related studies that examined *in-situ* FMDV aerosol stability of naturally
254 generated aerosols suggest that the lifetime of naturally generated aerosols is similarly
255 long. *Sellers et al.* [6] and *Sellers and Herniman* [56] examined the quantity of airborne
256 FMDV in animal holding pens (looseboxes) both prior to and after killing infected swine
257 and cattle.[14] Only the swine measurements are discussed in detail here as these
258 experiments were more extensive and the FMDV signal was higher (the results for cattle
259 also suggest a long aerosol lifetime). FMDV aerosol emissions were measured under four

[14] In *Sellers et al.* [6] sampling took place after the generalization of FMD. Lesion epithelium taken from swine feet during this experiment correspond to 10^9 $TCID_{50}$ per g of tissue. In *Sellers and Herniman* [56], sampling took place 48 and 72 hrs after inoculation and when generalized lesions were evident. Humidity was kept above 90%.

experimental conditions: a) in boxes in which live swine were held; b) in boxes in which live swine were placed and then removed (without being killed); c) in boxes in which live swine were placed and then killed (bodies remained in the box); and d) in clean boxes in which freshly killed swine bodies were placed. Overall (non-size resolved) airborne FMDV concentrations in swine holding pens were observed to decrease by 10 to 1,000 fold at 30 min and 24 hours, respectively, after live animals were removed (see *Supplemental Material*: *Supplemental Data Table 2* for more details). Separate measurements over a 1 hour time period suggest that most of the decrease in airborne infectivity was associated with large (>6 μm) aerosols and that for small (< 3 μm) aerosols, infectivity decreased less than 10 fold over a 1 hour time period. Gravitational settling of suspended aerosols could explain such loss rates[15] – indicating a limited loss rate (much less than 10x in 1 hr) of FMDV infectivity in airborne aerosols.

It is important to note that the aerosol stability estimates provided by these experiments do not provide any insight into the relative importance of the skin vs. respiratory emission sources. The experiments reported by *Sellers et al.* [6] and *Sellers and Herniman* [56] were performed at high (>90%) relative humidity. Laboratory experiments on synthetic aerosols generated from liquid FMDV suspensions have reported high-humidity aerosol decay rates that range from near 0 to 1,000 fold per hour depending on the virus strain and the suspending fluid used [57,58,59,60].

2.4. Aerosol Size

[15] Assuming the air within the 3 m high loosebox is well-mixed, gravitational settling would remove 30% of the 3 μm aerosols and 70% of the 6 μm aerosols in the first hour. After 24hrs, only 10^{-4} and 10^{-13} of the 3 μm and 6 μm original aerosol mass, respectively, would be expected to be remaining airborne.

The size fractionation typically reported for fresh FMD aerosol emissions is 10-30% in < 3 μm; 20 to 40 % in 3 to 6 μm; and 30 to 70% in >6 μm aerosols, respectively [5,7,51,56]. These measurements have been made in swine and no aerosol size fractionization distribution data appears to be available for cattle or sheep emissions. The measured size distribution for swine is consistent with what is known for mammalian skin cell aerosols – which are emitted in a variety of aerosol sizes but on average are large, ~14 μm (see the *Animal Skin Shedding Rate* section). In addition, if the measured loosebox aerosol loss rates derived from the *Sellers et al.* [6] and *Sellers and Herniman* [56] data (see *Supplemental Material: Supplemental Data Table 2*) are assumed to be due solely to gravitational settling, then the corresponding effective aerosol settling velocity, 0.3 m min^{-1}, agrees well with that found for skin aerosols [11,19]).

3. Discussion

3.1. Recommendations for Additional Experiments

The literature summarized above provides considerable evidence for the hypothesis that animal skin cells could be a significant source of infectious Foot and Mouth Disease virus aerosols. However, there are important knowledge gaps. Studies are outlined below that could significantly contribute to affirming or disproving this hypothesis.

First, the FMDV concentration in the outermost skin layer that normally exfoliates (stratum corneum) needs to be characterized. This could potentially be accomplished by analyzing skin samples from the bodies of infected animals using a skin surface sampling technique such as skin scraping (with care to select only the top layer of the epidermis) or

305 skin scrubbing [61]. Follow on work, if warranted, could characterize the (a) infectivity
306 and stability of FMDV in these skin cells, (b) degree to which infectious FMD in
307 exfoliated skin cells is intracellular vs. viral rafting on the surface, (c) emissions rate of
308 airborne infectious FMD skin cells, (d) infectious aerosols collected during whole animal
309 sampling, and (e) infectivity of environmentally aged, e.g. dust mite processed, skin
310 aerosols.
311
312 Second, the *Sellers et al.* [6] and *Sellers and Herniman* [56] experiments should be
313 repeated. These studies are unique (and therefore should be verified) because they are the
314 only experiments identified that examined (a) the FMDV aerosol emission rate from dead
315 animals, (b) the relative importance of respiratory vs. non-respiratory emission pathways
316 (suggested from the results of whole animal FMDV aerosol emissions from live and dead
317 animals), and (c) the time series of aerosol concentrations from whole animals when
318 animals were removed from the measurement chamber (this data was used to infer the
319 stability of infectious FMDV in natural aerosols). Key extensions to this work include the
320 use of domestic animals besides swine and testing in lower relative humidity
321 environments.
322
323 **3.2. Implications for Foot and Mouth Disease Control**
324 If further testing were to support the study hypothesis, then there are a number of
325 practical implications for FMD surveillance and control.
326

First, the sampling and management of settled dust could prove to be a useful tool for disease surveillance and control. Due to the (a) potentially high stability of FMDV in skin and (b) high fraction of exfoliated skin fragments in settled dust, FMDV could remain detectable (and indeed potentially infectious) in dust for months or years after a primary infection. The re-aerosolization of FMDV infected settled dust therefore could prove to be a significant concern (see *Supplemental Material: Particle Suspension Mechanisms*).

Second, slaughtered animals may still emit airborne FMDV via continued exfoliation of infected skin cells simply by exposure to air currents (e.g. wind) and/or external mechanical abrasion (e.g. moving animal carcasses, spraying hides with water).

Third, the current focus on swine airborne emissions (and the relative neglect of cattle and sheep emissions) may need to be revisited. It is well known that hair can trap aerosols. Of the three animals considered, pigs are known to be the highest FMD aerosol emitters and also have the lowest body hair count. Therefore while sheep (and to a lesser extent cattle) may typically have limited ability to shed skin aerosols through their coat into the atmosphere, shearing or similar actions that disturb the coat and/or skin could theoretically release infectious FMDV aerosols well after the obvious acute clinical infection has been cleared from the animal.

3.3. Implications for Other Diseases

If further work supports the study hypothesis with respect FMDV, the role of skin cell aerosols in spreading other viral diseases may be need to be revisited (see *Supplemental*

Material: Other Viral Diseases). Viral disease spread via skin cell aerosol is given minimal treatment or is entirely absent in recent literature reviews [62,63,64]. Given the potential for skin cells to provide protection to infectious virus against adverse environmental conditions, the management of several viral diseases may also benefit from enhanced dust surveillance and management and skin decontamination.

4. Summary and Conclusions

There is considerable evidence in the literature to support the hypothesis that infected animal skin cells could be a significant source of infectious Foot and Mouth Disease virus aerosols. **Table 3** provides a summary of both key findings and suggested future research.

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673 **Table Captions:**

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675 **Table 1 – Peak external skin FMDV concentrations**

676

677 **Table 2 – Peak whole-animal FMDV aerosol emission rates**

678

679 **Table 3 – Key study findings**

596 **Table 1 – Peak external skin FMDV concentrations**

sample location	cattle			swine			sheep		
	study	**average FMDV skin concentration (log10($TCID_{50}$)/g) [a]**	**number of measure-ments**	**study**	**average FMDV skin concentration (log10($TCID_{50}$)/g) [a]**	**number of measure-ments**	**study**	**average FMDV skin concentration (log10($TCID_{50}$)/g) [a]**	**number of measure-ments**
extremity lesion	[44]	7.4	2	[39]	9.5	2	[65]	8.4	5
				[48]	9.0	2			
				[45]	8.0	16			
	AVE	**7.4**		**AVE**	**8.8**		**AVE**	**8.4**	
extremity no lesion	[43]	6.4	11	[39]	6.0	4			
	[8]	4.0	21	[48]	6.5	n/a[b]			
	[44]	4.9	4						
	AVE	**5.1**		**AVE**	**6.3**		**AVE**	**n/a**	
non extremity	[43]	5.0	6	[45]	4.3	6			
	[8]	4.0	54						
	AVE	**4.5**		**AVE**	**4.3**		**AVE**	**n/a**	

597

598 [a] Units reported are $TCID_{50}$ - the amount of virus required to infect 50% of calf thyroid tissue (BTY) cultures [66]. Measurements reported using methods other
599 than BTY cultures have been scaled. Measurements reported below the instrument detection limits are assumed to be 0 for calculation purposes. See
600 Supplemental Data Table 1 for details.
601 [b] Scaled from lesion results based on data reported in *Monaghan et al* [48].
602

611 **Table 2 – Peak whole-animal FMDV aerosol emission rates**

612

cattle			swine			sheep		
study	**average peak FMDV aerosol emissions (log10($TCID_{50}$) per animal per day)**	**number of measure-ments**	**study**	**average peak FMDV aerosol emissions (log10($TCID_{50}$) per animal per day)**	**number of measure-ments**	**study**	**average peak FMDV aerosol emissions (log10($TCID_{50}$) per animal per day)**	**number of measure-ments**
[67]	4.0	4	[69]	6.9	2	[67]	5.2	1
[68]	4.1	9	[53]	7.6	1	[68]	2.7	8
[7]	4.7	3	[7]	6.4	2	[71]	5.4	1
[6]	4.4	3	[70]	7.3	8	[7]	4.1	2
			[68]	6.0	8			
			[52]	8.1	8			
			[51]	8.5	1			
			[6]	7.4	7			
AVE	**4.3**		**AVE**	**7.3**		**AVE**	**4.3**	

613

617

618 **Table 3 – Key study findings**

key finding	level of certainty	new data needed
Key Findings from Prior Studies		
FMDV is trophic for animal skin	Well Established	
Skin is a major secondary FMD viral replication site	Well Established	
FMDV is present both in skin lesions and in clinically normal appearing skin	Probable	
FMDV skin concentrations are highest in the epidermal layer	Probable	FMDV concentration & infectivity of apparently normal stratum corneum samples (analysis by species and body region).
In the normal skin growth cycle, epidermal skin cells are shed into the environment	Well Established	
Skin cells constitute a significant fraction of ambient aerosols and settled dust	Well Established	
Skin cell aerosols can deposit within the respiratory system	Probable	
Airborne skin cells are a known vehicle for disease transmission	Well established for Bacteria; Probable for Viruses (e.g. VZV)	Measurement of concentration and infectivity of FMDV on exfoliated skin cell surface and intra-cellularly in fresh and environmentally aged skin cells
Dead animals emit infectious aerosols	Probable	Confirmatory studies. Current data comes from a single study
Peak FMDV aerosol emissions are co-incident with peak FMDV skin concentrations	Well Established	
FMDV has high stability in detached (whole animal) skin	Probable	Confirmatory studies. Current data comes from two studies.
Key Findings from This Study		
Estimates of the peak FMDV infected animal skin cell shedding rate:		
- Are comparable to measured peak whole animal aerosol emissions	Probable	Skin cell shedding rates for domestic animals; Updated FMDV skin concentrations
- Exceed the minimum infectious dose by orders of magnitude	Possible	Degree to which FMDV is liberated from skin cells in the respiratory system
Stability of naturally generated infectious FMDV aerosols is consistent with that expected of FMDV infected skin aerosols	Possible	Confirmatory studies. Conclusion based on data from a single study and assumption that FMDV stability in skin aerosols is comparable to whole skin.
The whole animal FMDV infectious aerosol size distribution is consistent with that expected for skin cell aerosols	Well established	Enhanced characterization of (a) skin aerosol size distribution and (b) infectious whole animal FMDV aerosol size distribution
Utility of Study Hypothesis		
May point to new methods for FMD surveillance (e.g. settled dust)	Possible	Stability and infectivity of FMDV in dust
Potential to develop new, more effective disease control measures	Possible	Degree to which infected skin cells contribute to disease transmission
May lead to new studies on the persistence of the virus in the environment	Possible	Analysis of settled dust and other potential environmental resevoirs
May lead to better understanding of sources and vehicles of infectious aerosols with applicibility to other diseases	Possible	Degree to which infectious skin cells contribute to viral disease transmission

619

Supplemental Material: Other Viral Diseases

Manuscript Title: Skin as a Potential Source of Infectious Foot and Mouth Disease Aerosols

The biological plausibility of FMDV transmission via infectious skin cell is enhanced if a skin cell source of disease transmission has been established (or is likely) for other viruses. FMD is not the only viral pathogen for which (a) there is known skin trophism (e.g. rash or lesions), (b) the respiratory tract is known to be a significant (or dominant) infectious pathway, and (c) viral transmission is present co-incident with the skin trophism (often peaking with the skin trophism onset).[1] For example, airborne transmission of Marek's disease (a herpesviridae affecting poultry) is known to be associated with desquamated epidermal cells shed from feather follicles [S1]. In addition, a number of human viruses,[2] from several virus families, are well known to share these traits, including herpesviridae, e.g. Varicella-Zoster (chickenpox) [S2]; poxviridae, e.g. Variola Major and Minor (smallpox) [S3]; togaviridae, e.g. Rubivirus (rubella), and paramyxoviridae, e.g. Measles [S4].

Published data on Varicella-Zoster Virus (VZV) is particularly relevant to the current discussion. VZV is the cause of chickenpox and reactivation of dormant viral infection later in life causes localized cutaneous herpes zoster. VZV is believed to be transmitted by direct contact via fomites contaminated by the infected serous exudate from ruptured skin vesicles, but an important secondary route of transmission is hypothesized to be the airborne route via infected skin scales [S2].[3] VZV is detected in air samples taken from patient rooms and nearby locations. This is true both in room air samples for patients with widespread rashes (primary varicella) as well as in room air samples for cases presenting solely as a localized skin rash (reactivated local cutaneous herpes zoster) [S8,S9,S10,S11]. VZV DNA is also detected in environmental dust samples obtained up to 1.5 months after the clinical development of a rash [S11,S12]. *Suzuki et al.* [S10] demonstrated that when localized VZV rashes were covered with an impenetrable (hydrocolloid) dressing, viral samples from the patient's throat, the ambient room air, and outer surface of the dressing were nearly universally negative for VZV. In contrast, the corresponding samples from patients using standard gauze dressings (which are not expected to retard skin aerosol emissions) were nearly universally positive. Earlier work [S9] indicated that the sequence of positive virus detections progressed first from the patient's skin, then to ambient air samples and then to patient throat samples – suggesting that airborne VZV skin aerosols may be a source of disease transmission.

The data for variola major and minor (smallpox) is more circumstantial. The respiratory system is well-known to be the typical site of initial infection, but the aerosol generation pathway is not well understood [S3]. High viral levels are found in respiratory secretions during periods of high infectivity, suggesting a respiratory emission pathway. However, this period is also co-incident with the onset of the rash. Published studies [S13,S14] suggest that infectious aerosol emissions

[1] This screening criteria does not attempt to distinguish between infected material residing within or outside the skin cell aerosols (the latter would be expected from surface contamination via ruptured lesion).

[2] For human diseases, inhalation of virally infected skin cells may be a particularly efficient mechanism of disease transmission due to 1) the high (1 to 10%) fraction of indoor dust that is comprised of human skin fragments, 2) the large amount of time people spend indoors [S5], and 3) the known ability for large (>10 μm) aerosols to be inhaled by humans [S6].

[3] The degree to which respiratory emissions contribute to the overall disease transmission in primary VZV infection is still a point of debate [S7].

are primarily associated with relatively large aerosols (skin cell size) and the disturbance of bedsheets (which would harbor skin cells). Air samples taken near patients' mouths yielded relatively little virus. The composition of the carrier aerosol(s) has not been elucidated. We are unaware of a study that examined the concentration, lifetime, or infectivity of the variola virus in intact stratum corneum. However, it is well known that the variola virus can remain infectious for over 10 years in scab material, although scab-bound virus infectivity is low [S3].

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Supplemental Material: Supplemental Data Table 1

Author: M. B. Dillon

Manuscript Title: Skin as a Potential Source of Infectious Foot and Mouth Disease Aerosols

Auspices: This work performed under the auspices of the U.S. Department of Energy by Lawrence Livermore National Laboratory under Contract DE-AC52-07NA27

Species	Location	Study	Mean Value (log10(TCID50)/g)	Median Value (log10(TCID50)/g)	Number of Measurements
Cattle	Extremity w lesions	Zhang et al. [40]	7.4	7.4	2
	Extremity w/o lesions	Gailiunas [39]	6.4	6.5	11
		Gailiunas and Cottral [8]	4.0	4.6	21
		Zhang et al. [40]	4.9	5.0	4
		AVERAGE	**5.1**	**5.0**	
	Non-extremity	Gailiunas [39]	5.0	5.1	6
		Gailiunas and Cottral [8]	4.0	4.5	54
		AVERAGE	**4.5**	**4.8**	
Swine	Extremity w lesions	Alexandersen et al. [35]	9.5	9.5	2
		Monaghan et al. [42]	9.0	9.0	2
		Lee et al. [43]	8.0	10.2	16
		AVERAGE	**8.8**	**9.5**	
	Extremity w/o lesions	Alexandersen et al. [35]	6.0	6.0	4
		Monaghan et al. [42]	6.5	6.5	n/a *
		AVERAGE	**6.3**	**6.3**	
	Non-extremity	Lee et al. [43]	4.3	3.4	6
Sheep	Extremity w lesion	Ryan et al. [41]	8.4	8.4	5
	Unknown (extremity)	Ryan et al. [41]	7.7	8.0	4

* Based on comment that non-lesion tissue is 0.1 to 1% of lesion tissue

Study	Animal	Virus	Data Taken From	Reported Sample Location	Sample Location Category	Measurement Time (day post infection)	Measurement Type	Reported FMDV Skin Concentration (TCID50/g or RNA/g)	Normalizing Factor	Normalized Measurement (in BTY)		Notes
Alexandersen et al. [35]	Swine	O1 Lausanne Sw/65	Figure 4	Foot with lesions	Extremity lesion	3	PCR	1.00E+09	1	9.00		(a) TaqMan calibrated to BTY assay during study (calibrated values reported here); (b) clinical signs reported between days 3 and 4 dpi
Alexandersen et al. [35]	Swine	O1 Lausanne Sw/65	Figure 4	Foot with lesions	Extremity lesion	4	PCR	1.00E+10	1	10.00		(a) TaqMan calibrated to BTY assay during study (calibrated values reported here); (b) clinical signs reported between days 3 and 4 dpi
Alexandersen et al. [35]	Swine	O1 Lausanne Sw/65	Figure 4	Foot w/o lesions	Extremity no lesion	3	PCR	1.00E+06	1	6.00		(a) TaqMan calibrated to BTY assay during study (calibrated values reported here); (b) clinical signs reported between days 3 and 4 dpi
Alexandersen et al. [35]	Swine	O1 Lausanne Sw/65	Figure 4	Foot w/o lesions	Extremity no lesion	3	PCR	1.00E+06	1	6.00		(a) TaqMan calibrated to BTY assay during study (calibrated values reported here); (b) clinical signs reported between days 3 and 4 dpi
Alexandersen et al. [35]	Swine	O1 Lausanne Sw/65	Figure 4	Foot w/o lesions	Extremity no lesion	4	PCR	1.00E+06	1	6.00		(a) TaqMan calibrated to BTY assay during study (calibrated values reported here); (b) clinical signs reported between days 3 and 4 dpi
Alexandersen et al. [35]	Swine	O1 Lausanne Sw/65	Figure 4	Foot w/o lesions	Extremity no lesion	4	PCR	1.00E+06	1	6.00		(a) TaqMan calibrated to BTY assay during study (calibrated values reported here); (b) clinical signs reported between days 3 and 4 dpi
		SUMMARY			Extremity lesion					9.50	9.50	
		SUMMARY			Extremity no lesion					6.00	6.00	
Gailiunas [39]	Cattle	C-997	Table 3	Carpal	Extremity no lesion	1	bovine kidney culture	5.7	19.95262315	7.00		(a) clinical signs developed apprx 1 dpi
Gailiunas [39]	Cattle	C-997	Table 3	Hock	Extremity no lesion	1	bovine kidney culture	4.7	19.95262315	6.00		(a) clinical signs developed apprx 1 dpi
Gailiunas [39]	Cattle	C-997	Table 3	Brisket	Non-extremity	1	bovine kidney culture	2.3	19.95262315	3.60		(a) clinical signs developed apprx 1 dpi
Gailiunas [39]	Cattle	SAT-3 Bech	Table 3	Carpal	Extremity no lesion	1	bovine kidney culture	5.3	19.95262315	6.60		(a) clinical signs developed apprx 1 dpi
Gailiunas [39]	Cattle	SAT-3 Bech	Table 3	Hock	Extremity no lesion	1	bovine kidney culture	4.6	19.95262315	5.90		(a) clinical signs developed apprx 1 dpi
Gailiunas [39]	Cattle	SAT-3 Bech	Table 3	Brisket	Non-extremity	1	bovine kidney culture	3.5	19.95262315	4.80		(a) clinical signs developed apprx 1 dpi
Gailiunas [39]	Cattle	O-2	Table 3	Carpal	Extremity no lesion	4	bovine kidney culture	5.2	19.95262315	6.50		(a) clinical signs developed apprx 2-3 dpi
Gailiunas [39]	Cattle	O-2	Table 3	Hock	Extremity no lesion	4	bovine kidney culture	5.8	19.95262315	7.10		(a) clinical signs developed apprx 2-3 dpi
Gailiunas [39]	Cattle	O-2	Table 3	Brisket	Non-extremity	4	bovine kidney culture	4.5	19.95262315	5.80		(a) clinical signs developed apprx 2-3 dpi
Gailiunas [39]	Cattle	O-2	Table 3	Crural	Extremity no lesion	4	bovine kidney culture	3.8	19.95262315	5.10		(a) clinical signs developed apprx 2-3 dpi
Gailiunas [39]	Cattle	C-3	Table 3	Hock	Extremity no lesion	5	bovine kidney culture	5.3	19.95262315	6.60		(a) clinical signs developed apprx 2-3 dpi
Gailiunas [39]	Cattle	C-3	Table 3	Brisket	Non-extremity	5	bovine kidney culture	5	19.95262315	6.30		(a) clinical signs developed apprx 2-3 dpi
Gailiunas [39]	Cattle	C-3	Table 3	Tuber coxae	Non-extremity	5	bovine kidney culture	3	19.95262315	4.30		(a) clinical signs developed apprx 2-3 dpi
Gailiunas [39]	Cattle	A-4691	Table 3	Carpal	Extremity no lesion	5	bovine kidney culture	4.7	19.95262315	6.00		(a) clinical signs developed apprx 2-3 dpi
Gailiunas [39]	Cattle	A-4691	Table 3	Hock	Extremity no lesion	5	bovine kidney culture	6.7	19.95262315	8.00		(a) clinical signs developed apprx 2-3 dpi
Gailiunas [39]	Cattle	A-4691	Table 3	Brisket	Non-extremity	5	bovine kidney culture	4	19.95262315	5.30		(a) clinical signs developed apprx 2-3 dpi
Gailiunas [39]	Cattle	A-4691	Table 3	Crural	Extremity no lesion	5	bovine kidney culture	4	19.95262315	5.30		(a) clinical signs developed apprx 2-3 dpi
		SUMMARY			Extremity no lesion					6.37	6.50	
		SUMMARY			Non-extremity					5.02	5.05	

Study	Animal	Virus	Data Taken From	Reported Sample Location	Sample Location Category	Measurement Time (day post infection)	Measurement Type	Reported FMDV Skin Concentration (TCID50/g or RNA/g)	Normalizing Factor	Normalized Measurement (in BTY)		Notes
Gailiunas and Cottral [8]	Cattle	O-9	Table 2	Lumbar	Non-extremity	1	bovine kidney culture	0	19.95262315	1.30		(a) depending on innoculation route, clinical signs at 1 - 3 dpi (mostly 1 pdi)
Gailiunas and Cottral [8]	Cattle	O-2	Table 2	Lumbar	Non-extremity	1	bovine kidney culture	3.6	19.95262315	4.90		(a) depending on innoculation route, clinical signs at 1 - 3 dpi (mostly 1 pdi)
Gailiunas and Cottral [8]	Cattle	Asia-1	Table 2	Lumbar	Non-extremity	1	bovine kidney culture	3.8	19.95262315	5.10		(a) depending on innoculation route, clinical signs at 1 - 3 dpi (mostly 1 pdi)
Gailiunas and Cottral [8]	Cattle	SAT-2	Table 2	Lumbar	Non-extremity	2	bovine kidney culture	3.4	19.95262315	4.70		(a) depending on innoculation route, clinical signs at 1 - 3 dpi (mostly 1 pdi)
Gailiunas and Cottral [8]	Cattle	A-1	Table 2	Lumbar	Non-extremity	2	bovine kidney culture	3.2	19.95262315	4.50		(a) depending on innoculation route, clinical signs at 1 - 3 dpi (mostly 1 pdi)
Gailiunas and Cottral [8]	Cattle	SAT-3	Table 2	Lumbar	Non-extremity	2	bovine kidney culture	2	19.95262315	3.30		(a) depending on innoculation route, clinical signs at 1 - 3 dpi (mostly 1 pdi)
Gailiunas and Cottral [8]	Cattle	C-3	Table 2	Lumbar	Non-extremity	2	bovine kidney culture	4.7	19.95262315	6.00		(a) depending on innoculation route, clinical signs at 1 - 3 dpi (mostly 1 pdi)
Gailiunas and Cottral [8]	Cattle	SAT-1	Table 2	Lumbar	Non-extremity	3	bovine kidney culture	2.5	19.95262315	3.80		(a) depending on innoculation route, clinical signs at 1 - 3 dpi (mostly 1 pdi)
Gailiunas and Cottral [8]	Cattle	O-Mulder	Table 2	Lumbar	Non-extremity	3	bovine kidney culture	3	19.95262315	4.30		(a) depending on innoculation route, clinical signs at 1 - 3 dpi (mostly 1 pdi)
Gailiunas and Cottral [8]	Cattle	O-9	Table 2	Shoulder	Non-extremity	1	bovine kidney culture	0	19.95262315	1.30		(a) depending on innoculation route, clinical signs at 1 - 3 dpi (mostly 1 pdi)
Gailiunas and Cottral [8]	Cattle	O-2	Table 2	Shoulder	Non-extremity	1	bovine kidney culture	4.5	19.95262315	5.80		(a) depending on innoculation route, clinical signs at 1 - 3 dpi (mostly 1 pdi)
Gailiunas and Cottral [8]	Cattle	Asia-1	Table 2	Shoulder	Non-extremity	1	bovine kidney culture	0	19.95262315	1.30		(a) depending on innoculation route, clinical signs at 1 - 3 dpi (mostly 1 pdi)
Gailiunas and Cottral [8]	Cattle	SAT-2	Table 2	Shoulder	Non-extremity	2	bovine kidney culture	3.8	19.95262315	5.10		(a) depending on innoculation route, clinical signs at 1 - 3 dpi (mostly 1 pdi)
Gailiunas and Cottral [8]	Cattle	A-1	Table 2	Shoulder	Non-extremity	2	bovine kidney culture	0	19.95262315	1.30		(a) depending on innoculation route, clinical signs at 1 - 3 dpi (mostly 1 pdi)
Gailiunas and Cottral [8]	Cattle	SAT-3	Table 2	Shoulder	Non-extremity	2	bovine kidney culture	2	19.95262315	3.30		(a) depending on innoculation route, clinical signs at 1 - 3 dpi (mostly 1 pdi)
Gailiunas and Cottral [8]	Cattle	C-3	Table 2	Shoulder	Non-extremity	2	bovine kidney culture	4.6	19.95262315	5.90		(a) depending on innoculation route, clinical signs at 1 - 3 dpi (mostly 1 pdi)
Gailiunas and Cottral [8]	Cattle	SAT-1	Table 2	Shoulder	Non-extremity	3	bovine kidney culture	3.2	19.95262315	4.50		(a) depending on innoculation route, clinical signs at 1 - 3 dpi (mostly 1 pdi)
Gailiunas and Cottral [8]	Cattle	O-Mulder	Table 2	Shoulder	Non-extremity	3	bovine kidney culture	4	19.95262315	5.30		(a) depending on innoculation route, clinical signs at 1 - 3 dpi (mostly 1 pdi)
Gailiunas and Cottral [8]	Cattle	O-9	Table 2	Thigh	Extremity no lesion	1	bovine kidney culture	0	19.95262315	1.30		(a) depending on innoculation route, clinical signs at 1 - 3 dpi (mostly 1 pdi)
Gailiunas and Cottral [8]	Cattle	O-2	Table 2	Thigh	Extremity no lesion	1	bovine kidney culture	3.6	19.95262315	4.90		(a) depending on innoculation route, clinical signs at 1 - 3 dpi (mostly 1 pdi)
Gailiunas and Cottral [8]	Cattle	Asia-1	Table 2	Thigh	Extremity no lesion	1	bovine kidney culture	0	19.95262315	1.30		(a) depending on innoculation route, clinical signs at 1 - 3 dpi (mostly 1 pdi)
Gailiunas and Cottral [8]	Cattle	SAT-2	Table 2	Thigh	Extremity no lesion	2	bovine kidney culture	3.5	19.95262315	4.80		(a) depending on innoculation route, clinical signs at 1 - 3 dpi (mostly 1 pdi)
Gailiunas and Cottral [8]	Cattle	A-1	Table 2	Thigh	Extremity no lesion	2	bovine kidney culture	0	19.95262315	1.30		(a) depending on innoculation route, clinical signs at 1 - 3 dpi (mostly 1 pdi)
Gailiunas and Cottral [8]	Cattle	SAT-3	Table 2	Thigh	Extremity no lesion	2	bovine kidney culture	2	19.95262315	3.30		(a) depending on innoculation route, clinical signs at 1 - 3 dpi (mostly 1 pdi)
Gailiunas and Cottral [8]	Cattle	C-3	Table 2	Thigh	Extremity no lesion	2	bovine kidney culture	4.1	19.95262315	5.40		(a) depending on innoculation route, clinical signs at 1 - 3 dpi (mostly 1 pdi)
Gailiunas and Cottral [8]	Cattle	SAT-1	Table 2	Thigh	Extremity no lesion	3	bovine kidney culture	3.1	19.95262315	4.40		(a) depending on innoculation route, clinical signs at 1 - 3 dpi (mostly 1 pdi)
Gailiunas and Cottral [8]	Cattle	O-Mulder	Table 2	Thigh	Extremity no lesion	3	bovine kidney culture	3.2	19.95262315	4.50		(a) depending on innoculation route, clinical signs at 1 - 3 dpi (mostly 1 pdi)
Gailiunas and Cottral [8]	Cattle	O-9	Table 2	Perineal	Non-extremity	1	bovine kidney culture	5.5	19.95262315	6.80		(a) depending on innoculation route, clinical signs at 1 - 3 dpi (mostly 1 pdi)
Gailiunas and Cottral [8]	Cattle	O-2	Table 2	Perineal	Non-extremity	1	bovine kidney culture	4.5	19.95262315	5.80		(a) depending on innoculation route, clinical signs at 1 - 3 dpi (mostly 1 pdi)
Gailiunas and Cottral [8]	Cattle	Asia-1	Table 2	Perineal	Non-extremity	1	bovine kidney culture	0	19.95262315	1.30		(a) depending on innoculation route, clinical signs at 1 - 3 dpi (mostly 1 pdi)
Gailiunas and Cottral [8]	Cattle	SAT-2	Table 2	Perineal	Non-extremity	2	bovine kidney culture	3	19.95262315	4.30		(a) depending on innoculation route, clinical signs at 1 - 3 dpi (mostly 1 pdi)
Gailiunas and Cottral [8]	Cattle	A-1	Table 2	Perineal	Non-extremity	2	bovine kidney culture	0	19.95262315	1.30		(a) depending on innoculation route, clinical signs at 1 - 3 dpi (mostly 1 pdi)
Gailiunas and Cottral [8]	Cattle	SAT-3	Table 2	Perineal	Non-extremity	2	bovine kidney culture	1.5	19.95262315	2.80		(a) depending on innoculation route, clinical signs at 1 - 3 dpi (mostly 1 pdi)
Gailiunas and Cottral [8]	Cattle	C-3	Table 2	Perineal	Non-extremity	2	bovine kidney culture	0	19.95262315	1.30		(a) depending on innoculation route, clinical signs at 1 - 3 dpi (mostly 1 pdi)
Gailiunas and Cottral [8]	Cattle	SAT-1	Table 2	Perineal	Non-extremity	3	bovine kidney culture	4.3	19.95262315	5.60		(a) depending on innoculation route, clinical signs at 1 - 3 dpi (mostly 1 pdi)
Gailiunas and Cottral [8]	Cattle	O-Mulder	Table 2	Perineal	Non-extremity	3	bovine kidney culture	2.7	19.95262315	4.00		(a) depending on innoculation route, clinical signs at 1 - 3 dpi (mostly 1 pdi)
		SUMMARY			Extremity no lesion					3.47	4.40	
		SUMMARY			Non-extremity					3.89	4.30	
Gailiunas and Cottral [8]	Cattle	unknown	Table 3	Cheek	Non-extremity	1	bovine kidney culture	3.5	19.95262315	4.80		(a) animal may overlap with Table 2 data
Gailiunas and Cottral [8]	Cattle	unknown	Table 3	Lateral Neck	Non-extremity	1	bovine kidney culture	0	19.95262315	1.30		(a) animal may overlap with Table 2 data
Gailiunas and Cottral [8]	Cattle	unknown	Table 3	Ventral dewlap	Non-extremity	1	bovine kidney culture	4	19.95262315	5.30		(a) animal may overlap with Table 2 data
Gailiunas and Cottral [8]	Cattle	unknown	Table 3	Shoulder	Non-extremity	1	bovine kidney culture	4.5	19.95262315	5.80		(a) animal may overlap with Table 2 data
Gailiunas and Cottral [8]	Cattle	unknown	Table 3	Ventral Brisket	Non-extremity	1	bovine kidney culture	3.4	19.95262315	4.70		(a) animal may overlap with Table 2 data
Gailiunas and Cottral [8]	Cattle	unknown	Table 3	Dorsal Lumbar	Non-extremity	1	bovine kidney culture	3.6	19.95262315	4.90		(a) animal may overlap with Table 2 data
Gailiunas and Cottral [8]	Cattle	unknown	Table 3	Perineum	Non-extremity	1	bovine kidney culture	4.5	19.95262315	5.80		(a) animal may overlap with Table 2 data
Gailiunas and Cottral [8]	Cattle	unknown	Table 3	Ventral Udder	Non-extremity	1	bovine kidney culture	3.8	19.95262315	5.10		(a) animal may overlap with Table 2 data
Gailiunas and Cottral [8]	Cattle	unknown	Table 3	Ventral Abdomen	Non-extremity	1	bovine kidney culture	0	19.95262315	1.30		(a) animal may overlap with Table 2 data
Gailiunas and Cottral [8]	Cattle	unknown	Table 3	Inner Thigh	Extremity no lesion	1	bovine kidney culture	3.6	19.95262315	4.90		(a) animal may overlap with Table 2 data
Gailiunas and Cottral [8]	Cattle	unknown	Table 3	Achilles Insertion	Extremity no lesion	1	bovine kidney culture	4.4	19.95262315	5.70		(a) animal may overlap with Table 2 data
Gailiunas and Cottral [8]	Cattle	unknown	Table 3	Anterior Carpus	Extremity no lesion	1	bovine kidney culture	0	19.95262315	1.30		(a) animal may overlap with Table 2 data
Gailiunas and Cottral [8]	Cattle	unknown	Table 3	First Phalnax	Extremity no lesion	1	bovine kidney culture	0	19.95262315	1.30		(a) animal may overlap with Table 2 data
Gailiunas and Cottral [8]	Cattle	unknown	Table 3	Cheek	Non-extremity	2	bovine kidney culture	3.8	19.95262315	5.10		(a) animal may overlap with Table 2 data
Gailiunas and Cottral [8]	Cattle	unknown	Table 3	Lateral Neck	Non-extremity	2	bovine kidney culture	2.5	19.95262315	3.80		(a) animal may overlap with Table 2 data
Gailiunas and Cottral [8]	Cattle	unknown	Table 3	Ventral dewlap	Non-extremity	2	bovine kidney culture	3.2	19.95262315	4.50		(a) animal may overlap with Table 2 data
Gailiunas and Cottral [8]	Cattle	unknown	Table 3	Shoulder	Non-extremity	2	bovine kidney culture	2.5	19.95262315	3.80		(a) animal may overlap with Table 2 data
Gailiunas and Cottral [8]	Cattle	unknown	Table 3	Ventral Brisket	Non-extremity	2	bovine kidney culture	3.5	19.95262315	4.80		(a) animal may overlap with Table 2 data
Gailiunas and Cottral [8]	Cattle	unknown	Table 3	Dorsal Lumbar	Non-extremity	2	bovine kidney culture	4	19.95262315	5.30		(a) animal may overlap with Table 2 data
Gailiunas and Cottral [8]	Cattle	unknown	Table 3	Perineum	Non-extremity	2	bovine kidney culture	3.2	19.95262315	4.50		(a) animal may overlap with Table 2 data
Gailiunas and Cottral [8]	Cattle	unknown	Table 3	Ventral Udder	Non-extremity	2	bovine kidney culture	0	19.95262315	1.30		(a) animal may overlap with Table 2 data
Gailiunas and Cottral [8]	Cattle	unknown	Table 3	Ventral Abdomen	Non-extremity	2	bovine kidney culture	3.6	19.95262315	4.90		(a) animal may overlap with Table 2 data
Gailiunas and Cottral [8]	Cattle	unknown	Table 3	Inner Thigh	Extremity no lesion	2	bovine kidney culture	3.3	19.95262315	4.60		(a) animal may overlap with Table 2 data
Gailiunas and Cottral [8]	Cattle	unknown	Table 3	Achilles Insertion	Extremity no lesion	2	bovine kidney culture	3.7	19.95262315	5.00		(a) animal may overlap with Table 2 data
Gailiunas and Cottral [8]	Cattle	unknown	Table 3	Anterior Carpus	Extremity no lesion	2	bovine kidney culture	4.9	19.95262315	6.20		(a) animal may overlap with Table 2 data
Gailiunas and Cottral [8]	Cattle	unknown	Table 3	First Phalnax	Extremity no lesion	2	bovine kidney culture	3.4	19.95262315	4.70		(a) animal may overlap with Table 2 data
Gailiunas and Cottral [8]	Cattle	unknown	Table 3	Cheek	Non-extremity	3	bovine kidney culture	3.5	19.95262315	4.80		(a) animal may overlap with Table 2 data
Gailiunas and Cottral [8]	Cattle	unknown	Table 3	Lateral Neck	Non-extremity	3	bovine kidney culture	1.8	19.95262315	3.10		(a) animal may overlap with Table 2 data
Gailiunas and Cottral [8]	Cattle	unknown	Table 3	Ventral dewlap	Non-extremity	3	bovine kidney culture	4.6	19.95262315	5.90		(a) animal may overlap with Table 2 data
Gailiunas and Cottral [8]	Cattle	unknown	Table 3	Shoulder	Non-extremity	3	bovine kidney culture	3.2	19.95262315	4.50		(a) animal may overlap with Table 2 data
Gailiunas and Cottral [8]	Cattle	unknown	Table 3	Ventral Brisket	Non-extremity	3	bovine kidney culture	0	19.95262315	1.30		(a) animal may overlap with Table 2 data
Gailiunas and Cottral [8]	Cattle	unknown	Table 3	Dorsal Lumbar	Non-extremity	3	bovine kidney culture	2.5	19.95262315	3.80		(a) animal may overlap with Table 2 data
Gailiunas and Cottral [8]	Cattle	unknown	Table 3	Perineum	Non-extremity	3	bovine kidney culture	4.3	19.95262315	5.60		(a) animal may overlap with Table 2 data
Gailiunas and Cottral [8]	Cattle	unknown	Table 3	Ventral Udder	Non-extremity	3	bovine kidney culture	0	19.95262315	1.30		(a) animal may overlap with Table 2 data
Gailiunas and Cottral [8]	Cattle	unknown	Table 3	Ventral Abdomen	Non-extremity	3	bovine kidney culture	2.8	19.95262315	4.10		(a) animal may overlap with Table 2 data
Gailiunas and Cottral [8]	Cattle	unknown	Table 3	Inner Thigh	Extremity no lesion	3	bovine kidney culture	3.1	19.95262315	4.40		(a) animal may overlap with Table 2 data
Gailiunas and Cottral [8]	Cattle	unknown	Table 3	Achilles Insertion	Extremity no lesion	3	bovine kidney culture	0	19.95262315	1.30		(a) animal may overlap with Table 2 data
Gailiunas and Cottral [8]	Cattle	unknown	Table 3	Anterior Carpus	Extremity no lesion	3	bovine kidney culture	4	19.95262315	5.30		(a) animal may overlap with Table 2 data
Gailiunas and Cottral [8]	Cattle	unknown	Table 3	First Phalnax	Extremity no lesion	3	bovine kidney culture	5.8	19.95262315	7.10		(a) animal may overlap with Table 2 data
		SUMMARY			Extremity no lesion					4.32	4.80	
		SUMMARY			Non-extremity					4.13	4.70	
Gailiunas and Cottral [8]		SUMMARY	Combined Table 2 & 3 data		Extremity no lesion					3.95	4.60	
Gailiunas and Cottral [8]		SUMMARY	Combined Table 2 & 3 data		Non-extremity					4.01	4.50	

Study	Animal	Virus	Data Taken From	Reported Sample Location	Sample Location Category	Measurement Time (day post infection)	Measurement Type	Reported FMDV Skin Concentration (TCID50/g or RNA/g)	Normalizing Factor	Normalized Measurement (in BTY)		Notes
Monaghan et al. [42]	swine	O UKG 34/2001	Table 1	Coronary band	Extremity lesion	2	PCR	11.5	0.003333333	9.02		(a) clinical lesions arise 1 to 2 dpi
Monaghan et al. [42]	swine	O UKG 34/2001	Table 1	Coronary band	Extremity lesion	2	PCR	11.5	0.003333333	9.02		(a) clinical lesions arise 1 to 2 dpi
Monaghan et al. [42]	swine	loads in non-lesion skin "in general" 0.1 to 1% of vesicular lesion based on unpublished findings (p. 6413) ; non lesion viral loads not measured										
Ryan et al. [41]	sheep	O UKG 34/2001	Table 1	Coronary band (unk	Extremity lesion	2	PCR	9.05	0.003333333	6.57		(a) innoculated ewe (presumed lesion, clinical signs reported); (b) clinical signs at 1-2 dpi (1 dpi data not available)
Ryan et al. [41]	sheep	O UKG 34/2001	Table 1	Coronary band (unk	Extremity lesion	3	PCR	8.7	0.003333333	6.22		(a) innoculated ewe (presumed lesion, clinical signs reported); (b) clinical signs at 1-2 dpi (1 dpi data not available)
Ryan et al. [41]	sheep	O UKG 34/2001	Table 2	Coronary band (unk	Unknown	4	PCR	8.77	0.003333333	6.29		(a) contact ewe; (b) viraemia s at 2-3 dpi (no 3 dpi data available), no clinical signs provided; (c) high levels still seen at 7-10 dpi
Ryan et al. [41]	sheep	O UKG 34/2001	Table 2	Coronary band (unk	Unknown	4	PCR	10.45	0.003333333	7.97		(a) contact ewe; (b) viraemia s at 2-3 dpi (no 3 dpi data available), no clinical signs provided; (c) high levels still seen at 7-10 dpi
Ryan et al. [41]	sheep	O UKG 34/2001	Table 4	Coronary band (unk	Extremity lesion	2	PCR	13.43	0.003333333	10.95		(a) innoculated lambs; (b) clinical at 1 dpi
Ryan et al. [41]	sheep	O UKG 34/2001	Table 4	Coronary band (unk	Extremity lesion	2	PCR	12.41	0.003333333	9.93		(a) innoculated lambs; (b) clinical at 1 dpi
Ryan et al. [41]	sheep	O UKG 34/2001	Table 4	Lateral hindleg	Unknown	2	PCR	11.01	0.003333333	8.53		(a) innoculated lambs; (b) clinical at 1 dpi
Ryan et al. [41]	sheep	O UKG 34/2001	Table 4	Lateral hindleg	Unknown	2	PCR	10.44	0.003333333	7.96		(a) innoculated lambs; (b) clinical at 1 dpi
Ryan et al. [41]	sheep	O UKG 34/2001	Table 5	Coronary band (unk	Extremity lesion	3	PCR	10.89	0.003333333	8.41		(a) contact lamb; (b) first day of lesions
		SUMMARY			Unknown					7.69	7.97	
		SUMMARY			Extremity lesion					8.42	8.41	
Zhang et al. [40]	cattle	O UKG 34/2001	Table 2	Interdigital area or o	Extremity no lesion	1	PCR	8.3	0.003333333	5.82		(a) direct innoculation; (b) clinical signs approx 1-2 dpi
Zhang et al. [40]	cattle	O UKG 34/2001	Table 2	Interdigital area or o	Extremity no lesion	1	PCR	8.43	0.003333333	5.95		(a) direct innoculation; (b) clinical signs approx 1-2 dpi
Zhang et al. [40]	cattle	O UKG 34/2001	Table 2	Interdigital area or o	Extremity no lesion	3	PCR	6.19	0.003333333	3.71		(a) direct innoculation; (b) clinical signs approx 1-2 dpi
Zhang et al. [40]	cattle	O UKG 34/2001	Table 2	Interdigital area or o	Extremity no lesion	3	PCR	6.73	0.003333333	4.25		(a) direct innoculation; (b) clinical signs approx 1-2 dpi
Zhang et al. [40]	cattle	O UKG 34/2001	Table 2	Interdigital area or o	Extremity lesion	3	PCR	10.02	0.003333333	7.54		(a) direct innoculation; (b) clinical signs approx 1-2 dpi
Zhang et al. [40]	cattle	O UKG 34/2001	Table 2	Interdigital area or o	Extremity lesion	3	PCR	9.7	0.003333333	7.22		(a) direct innoculation; (b) clinical signs approx 1-2 dpi
		SUMMARY			Extremity no lesion					4.94	5.04	
		SUMMARY			Extremity lesion					7.38	7.38	
Lee et al. [43]	swine	O/Taiwan/97	Table 1	L Ant Heel Bulb	Extremity lesion	2	Baby Hamster Kidney - 21	8.63	1000	11.63		(a) lesions found at non-innoculation site at 2 dpi; (b) nominal scaling factor (O TAW 97 is known not to grow well in BTY)
Lee et al. [43]	swine	O/Taiwan/97	Table 1	L Ant Heel Bulb	Extremity lesion	2	Baby Hamster Kidney - 21	7.5	1000	10.50		(a) lesions found at non-innoculation site at 2 dpi; (b) nominal scaling factor (O TAW 97 is known not to grow well in BTY)
Lee et al. [43]	swine	O/Taiwan/97	Table 1	L Ant Cor Band	Extremity lesion	2	Baby Hamster Kidney - 21	7.4	1000	10.40		(a) lesions found at non-innoculation site at 2 dpi; (b) nominal scaling factor (O TAW 97 is known not to grow well in BTY)
Lee et al. [43]	swine	O/Taiwan/97	Table 1	L Ant Cor Band	Extremity lesion	2	Baby Hamster Kidney - 21	7.5	1000	10.50		(a) lesions found at non-innoculation site at 2 dpi; (b) nominal scaling factor (O TAW 97 is known not to grow well in BTY)
Lee et al. [43]	swine	O/Taiwan/97	Table 1	R post heel bulb	Extremity lesion	2	Baby Hamster Kidney - 21	6.5	1000	9.50		(a) lesions found at non-innoculation site at 2 dpi; (b) nominal scaling factor (O TAW 97 is known not to grow well in BTY)
Lee et al. [43]	swine	O/Taiwan/97	Table 1	R post heel bulb	Extremity lesion	2	Baby Hamster Kidney - 21	0	1000	0.00		(a) lesions found at non-innoculation site at 2 dpi; (b) nominal scaling factor (O TAW 97 is known not to grow well in BTY)
Lee et al. [43]	swine	O/Taiwan/97	Table 1	R post cor band	Extremity lesion	2	Baby Hamster Kidney - 21	6.6	1000	9.60		(a) lesions found at non-innoculation site at 2 dpi; (b) nominal scaling factor (O TAW 97 is known not to grow well in BTY)
Lee et al. [43]	swine	O/Taiwan/97	Table 1	R post cor band	Extremity lesion	2	Baby Hamster Kidney - 21	0	1000	0.00		(a) lesions found at non-innoculation site at 2 dpi; (b) nominal scaling factor (O TAW 97 is known not to grow well in BTY)
Lee et al. [43]	swine	O/Taiwan/97	Table 1	L post heel bulb	Extremity lesion	2	Baby Hamster Kidney - 21	7	1000	10.00		(a) lesions found at non-innoculation site at 2 dpi; (b) nominal scaling factor (O TAW 97 is known not to grow well in BTY)
Lee et al. [43]	swine	O/Taiwan/97	Table 1	L post heel bulb	Extremity lesion	2	Baby Hamster Kidney - 21	0	1000	0.00		(a) lesions found at non-innoculation site at 2 dpi; (b) nominal scaling factor (O TAW 97 is known not to grow well in BTY)
Lee et al. [43]	swine	O/Taiwan/97	Table 1	L post cor band	Extremity lesion	2	Baby Hamster Kidney - 21	7.4	1000	10.40		(a) lesions found at non-innoculation site at 2 dpi; (b) nominal scaling factor (O TAW 97 is known not to grow well in BTY)
Lee et al. [43]	swine	O/Taiwan/97	Table 1	L post cor band	Extremity lesion	2	Baby Hamster Kidney - 21	8.63	1000	11.63		(a) lesions found at non-innoculation site at 2 dpi; (b) nominal scaling factor (O TAW 97 is known not to grow well in BTY)
Lee et al. [43]	swine	O/Taiwan/97	Table 1	Snout	Extremity lesion	2	Baby Hamster Kidney - 21	8.63	1000	11.63		(a) lesions found at non-innoculation site at 2 dpi; (b) nominal scaling factor (O TAW 97 is known not to grow well in BTY)
Lee et al. [43]	swine	O/Taiwan/97	Table 1	Snout	Extremity lesion	2	Baby Hamster Kidney - 21	7	1000	10.00		(a) lesions found at non-innoculation site at 2 dpi; (b) nominal scaling factor (O TAW 97 is known not to grow well in BTY)
Lee et al. [43]	swine	O/Taiwan/97	Table 1	Lip	Extremity lesion	2	Baby Hamster Kidney - 21	8.63	1000	11.63		(a) lesions found at non-innoculation site at 2 dpi; (b) nominal scaling factor (O TAW 97 is known not to grow well in BTY)
Lee et al. [43]	swine	O/Taiwan/97	Table 1	Lip	Extremity lesion	2	Baby Hamster Kidney - 21	0	1000	0.00		(a) lesions found at non-innoculation site at 2 dpi; (b) nominal scaling factor (O TAW 97 is known not to grow well in BTY)
Lee et al. [43]	swine	O/Taiwan/97	Table 1	teat	Non-extremity	2	Baby Hamster Kidney - 21	6.2	1000	9.20		(a) lesions found at non-innoculation site at 2 dpi; (b) nominal scaling factor (O TAW 97 is known not to grow well in BTY)
Lee et al. [43]	swine	O/Taiwan/97	Table 1	teat	Non-extremity	2	Baby Hamster Kidney - 21	0	1000	0.00		(a) lesions found at non-innoculation site at 2 dpi; (b) nominal scaling factor (O TAW 97 is known not to grow well in BTY)
Lee et al. [43]	swine	O/Taiwan/97	Table 1	Ear Tip	Non-extremity	2	Baby Hamster Kidney - 21	6.6	1000	9.60		(a) lesions found at non-innoculation site at 2 dpi; (b) nominal scaling factor (O TAW 97 is known not to grow well in BTY)
Lee et al. [43]	swine	O/Taiwan/97	Table 1	Ear Tip	Non-extremity	2	Baby Hamster Kidney - 21	3.8	1000	6.80		(a) lesions found at non-innoculation site at 2 dpi; (b) nominal scaling factor (O TAW 97 is known not to grow well in BTY)
Lee et al. [43]	swine	O/Taiwan/97	Table 1	Scrotum Epi	Non-extremity	2	Baby Hamster Kidney - 21	0	1000	0.00		(a) lesions found at non-innoculation site at 2 dpi; (b) nominal scaling factor (O TAW 97 is known not to grow well in BTY)
Lee et al. [43]	swine	O/Taiwan/97	Table 1	Scrotum Epi	Non-extremity	2	Baby Hamster Kidney - 21	0	1000	0.00		(a) lesions found at non-innoculation site at 2 dpi; (b) nominal scaling factor (O TAW 97 is known not to grow well in BTY)
		SUMMARY			Extremity lesion					7.96	10.20	
		SUMMARY			Non-extremity					4.27	3.40	

Raw Data

From Donaldson et al. [54], Table 1 — Units: log10(TCID50/mL)

	O1 BFS 1860	O2 Brecnia	A5 Eystrup	A22 Iraq	C Lebanon	C Nov
Calf Thyroid (	7.7	6.5	7.1	7.1	8.1	8.3
BHK-21	4.4	4.3	2.84	4.5	6.1	2.1
IB-RS-2	4.95	4.45	2.49	5.1	6.6	4.3
Calf Kidney	6.1	5.1	5.7	5.5	7.2	7.55

From Alexandersen and Donaldson [53] — Units: log10(TCID50/mL)

	O UKG 24/2001	O1 Lausanne	O SKR
Calf Thyroid (	8.8	6.7	6.45
IB-RS-2	7.6	5.7	5.7

From Alexanderson et al. [50] — Units: log10(TCID50/mL)

	O UKG 24/2001	O TAW 1997
Calf Thyroid (	7.2	authors noted that grows "poorly" in BTY
IB-RS-2	6.2	

PCR to BTY ratio is 100 to 1000 in serum for O UKG 24/2001, early period nasal swabs ~1,000

From Alexanderson et al. [52] — Units: log10(TCID50/mL)

	O UKG 24/2001
CalkfThyroid (	8.8
IB-RS-2	7.6

Ratio of Method to Calf Thyroic

Units: Log10(TCID50) increase for BTY over specified method

	O1 BFS 1860	O2 Brecnia	A5 Eystrup	A22 Iraq	C Lebanon	C Nov
BHK-21	3.3	2.2	4.26	2.6	2	6.2
IB-RS-2	2.75	2.05	4.61	2	1.5	4
Calf Kidney	1.6	1.4	1.4	1.6	0.9	0.75

Units: Log10(TCID50) increase for BTY over specified method

	O UKG 24/2001	O1 Lausanne Sw/65	O SKR
IB-RS-2	1.2	1	0.75

Units: Log10(TCID50) increase for BTY over specified method

	O UKG 24/2001
IB-RS-2	1
PCR	-2.5

Units: Log10(TCID50) increase for BTY over specified method

	O UKG 24/2001
IB-RS-2	1.2

Summary of Scaling Values Used

Base Assay	Ratio [BTY]/[Base Assay]
BHK-21	1000
IB-RS-2	50
Calf Kidney	19.95262
PCR	0.003333

Supplemental Material: Supplemental Data Table 2

Author: M. B. Dillon

Manuscript Title: Skin as a Potential Source of Infectious Foot and Mouth Disease Aerosols

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Species	Study	Mean Value (log10(TCID50)/animal/day)	Median Value (log10(TCID50)/animal/day)	Number of Measurements
Cattle	Alexandersen et al. [52]	4.0	5.3	4
	Donaldson et al. [54]	4.1	4.5	9
	Sellers and Parker [7]	4.7	4.5	3
	Sellers et al. [6]	4.4	4.4	3
	AVERAGE	**4.3**	**4.5**	
Swine	Alexandersen and Donaldson [53]	6.9	6.9	2
	Alexandersen et al. [50]	7.6	7.6	1
	Sellers and Parker [7]	6.4	6.4	2
	Donaldson et al. [56]	7.3	7.4	8
	Donaldson et al. [54]	6.0	6.2	8
	Gloster et al. [49]	8.1	8.2	8
	Gloster et al. [48]	8.5	8.5	1
	Sellers et al. [6]	7.4	7.5	7
	AVERAGE	**7.3**	**7.5**	
Sheep	Alexandersen et al. [52]	5.2	5.2	1
	Donaldson et al. [54]	2.7	3.0	8
	Esteves et al. [55]	5.4	5.4	1
	Sellers and Parker [7]	4.1	4.1	2
	AVERAGE	**4.3**	**4.6**	

Study	Animal	Virus Type	Total Virus Collected on Sampling Media (TCID50)	Assay Type	Sampling Rate (Lpm)	Collection Time (hr)	Measurement Time (Day Post Infection)	Virus Concentration in Loosebox Air (TCID50/L)	Number of Animals Sampled	Air Exchange Rate in Loosebox (ACH)	Per Animal Airborne Virus Emission Rate (TCID50/animal/hour)	(log10(TCID50)/animal/day)	
Alexandersen and Donaldson [53]	Swine	O UKG 34/2001	unknown	BTY	170	0.333333333	2	2.49	3	4	298800	6.9	
Alexandersen and Donaldson [53]	Swine	O UKG 34/2001	unknown	BTY	170	0.333333333	2	2.49	3	4	298800	6.9	
											SUMMARY 6.9		6.9
Alexandersen et al. [50]	Swine	C Noville		BTY				7.4	2	7.943282347	1857245.209	7.6	
Sellers and Parker [7]	Swine	O_1 Lombardy; O1 Swiss 1/66; O1 BFS 1860; O2 Brescia	50118.72336 mice	BTY, Unweaned	1000	1	1.708333333	0.835312056	1	0	180427.4041	6.6	
Sellers and Parker [7]	Swine	O_1 Lombardy; O1 Swiss 1/66; O1 BFS 1860; O2 Brescia	19952.62315 mice	BTY, Unweaned	1000	1	2.708333333	0.332543719	1	0	71829.44334	6.2	
											SUMMARY 6.4		6.4
Donaldson et al. [56]	Swine	C Noville	3162277.66	BTY	1000	0.5	unknown	105.4092553	8	0	2846049.894	7.8	
Donaldson et al. [56]	Swine	C Noville	1995262.315	BTY	1000	0.5	unknown	66.50874383	8	0	1795736.083	7.6	
Donaldson et al. [56]	Swine	C Noville	3162277.66	BTY	1000	0.5	unknown	105.4092553	8	0	2846049.894	7.8	
Donaldson et al. [56]	Swine	C Noville	501187.2336	BTY	1000	0.5	unknown	16.70624112	8	0	451068.5103	7.0	
Donaldson et al. [56]	Swine	C Noville	199526.2315	BTY	1000	0.5	unknown	6.650874383	5	0	287317.7734	6.8	
Donaldson et al. [56]	Swine	C Noville	50118.72336	BTY	1000	0.5	unknown	1.670624112	5	0	72170.96164	6.2	
Donaldson et al. [56]	Swine	C Noville	1995262.315	BTY	1000	0.5	unknown	66.50874383	5	0	2873177.734	7.8	
Donaldson et al. [56]	Swine	C Noville	398107.1706	BTY	1000	0.5	unknown	13.27023902	5	0	573274.3256	7.1	
											SUMMARY 7.3		7.4
Donaldson et al. [54]	Swine	A5	1258.925412	BTY	1000	1	2	0.02098209	1	0	4532.131482	5.0	
Donaldson et al. [54]	Swine	A22	17782.7941	BTY	1000	1	2	0.296379902	1	0	64018.05876	6.2	
Donaldson et al. [54]	Swine	C Lebanon	22387.21139	BTY	1000	1	2	0.37312019	1	0	80593.96099	6.3	
Donaldson et al. [54]	Swine	C Noville	199526.2315	BTY	1000	1	2	3.325437192	1	0	718294.4334	7.2	
Donaldson et al. [54]	Swine	A5	707.9457844	BTY	1000	1	3	0.011799096	1	0	2548.604824	4.8	
Donaldson et al. [54]	Swine	A22	3162.27766	BTY	1000	1	3	0.052704628	1	0	11384.19958	5.4	
Donaldson et al. [54]	Swine	C Lebanon	22387.21139	BTY	1000	1	3	0.37312019	1	0	80593.96099	6.3	
Donaldson et al. [54]	Swine	C Noville	79432.82347	BTY	1000	1	3	1.323880391	1	0	285958.1645	6.8	
											SUMMARY 6.0		6.2
Gloster et al. [49]	Swine	O UKG 34/2001		BTY			2	25.64102564	5	18	4430769.231	8.0	
Gloster et al. [49]	Swine	O UKG 34/2001		BTY			2	51.16057218	5	18	8840546.872	8.3	
Gloster et al. [49]	Swine	C Noville		BTY			2	10.20787617	5	18	1763921.002	7.6	
Gloster et al. [49]	Swine	C Noville		BTY			2	64.4073444	5	18	11129589.11	8.4	
Gloster et al. [49]	Swine	O UKG 34/2001		BTY			3	128.5095471	5	18	22206449.74	8.7	
Gloster et al. [49]	Swine	O UKG 34/2001		BTY			3	3.228013876	5	18	557800.7978	7.1	
Gloster et al. [49]	Swine	C Noville		BTY			3	161.7839345	5	18	27956263.88	8.8	
Gloster et al. [49]	Swine	C Noville		BTY			3	20.36739063	5	18	3519485.102	7.9	
											SUMMARY 8.1		8.2
Gloster et al. [48]	Swine	O UKG 34/2001		BTY			2	102.0787617	5	10	11759473.35	8.5	
Sellers et al. [6]	Swine	O1 Swiss 1/66	251188.6432	BTY	1000	0.75	unknown	5.581969848	8	0	150713.1859	6.6	
Sellers et al. [6]	Swine	C Noville	15848931.92	BTY	1000	0.5	unknown	528.2977308	8	0	14264038.73	8.5	
Sellers et al. [6]	Swine	O1 BFS 1860	125892.5412	BTY	1000	0.5	unknown	4.196418038	6	0	151071.0494	6.6	
Sellers et al. [6]	Swine	C Noville	1584893.192	BTY	1000	0.5	unknown	52.82977308	8	0	1426403.873	7.5	
Sellers et al. [6]	Swine	O1 BFS 1860	316227.766	BTY	1000	0.5	unknown	10.54092553	8	0	284604.9894	6.8	
Sellers et al. [6]	Swine	C Noville	3981071.706	BTY	1000	0.5	unknown	132.7023902	8	0	3582964.535	7.9	
Sellers et al. [6]	Swine	O1 BFS 1860	316227.66	BTY	1000	0.5	unknown	105.4092553	8	0	2846049.894	7.8	
											SUMMARY 7.4		7.5
Alexandersen et al. [52]	Cattle	O UKG 34/2001	252	BTY	170	0.333333333	1	0.074117647	2	3	12007.05882	5.5	
Alexandersen et al. [52]	Cattle	O UKG 34/2001	100	BTY	170	0.333333333	1	0.029411765	2	3	4764.705882	5.1	
Alexandersen et al. [52]	Cattle	O UKG 34/2001	252	BTY	170	0.333333333	3	0.074117647	2	3	12007.05882	5.5	
Alexandersen et al. [52]	Cattle	O UKG 34/2001	0	BTY	170	0.333333333	3	0	2	3	0	0.0	
											SUMMARY 4.0		5.3
Donaldson et al. [54]	Cattle	C Lebanon	398.1071706	BTY, unweaned	1000	1	2	0.00663512	1	0	1433.185814	4.5	
Donaldson et al. [54]	Cattle	C Noville	199.5262315	BTY, unweaned	1000	1	2	0.003325437	1	0	718.2944334	4.2	
Donaldson et al. [54]	Cattle	A5	398.1071706	BTY, unweaned	1000	1	2	0.00663512	1	0	1433.185814	4.5	
Donaldson et al. [54]	Cattle	C Lebanon	398.1071706	BTY, unweaned	1000	1	3	0.00663512	1	0	1433.185814	4.5	
Donaldson et al. [54]	Cattle	C Noville	1995.262315	BTY, unweaned	1000	1	3	0.033254372	1	0	7182.944334	5.2	
Donaldson et al. [54]	Cattle	A5	281.8382931	BTY, unweaned	1000	1	3	0.004697305	1	0	1014.617855	4.4	
Donaldson et al. [54]	Cattle	A22	354.8133892	BTY, unweaned	1000	1	3	0.005913556	1	0	1277.328201	4.5	
Donaldson et al. [54]	Cattle	A22	562.3413252	BTY, unweaned	1000	1	4	0.009372355	1	0	2024.428771	4.7	
Donaldson et al. [54]	Cattle	A22	0	BTY, unweaned	1000	1	4	0	1	0	0	0.0	
											SUMMARY 4.1		4.5
Sellers and Parker [7]	Cattle	O_1 Lombardy; O1 Swiss 1/66; O1 BFS 1860; O2 Brescia	1584.893192 mice	BTY, Unweaned	1000	1	1.708333333	0.026414887	1	0	5705.615493	5.1	
Sellers and Parker [7]	Cattle	O_1 Lombardy; O1 Swiss 1/66; O1 BFS 1860; O2 Brescia	398.1071706 mice	BTY, Unweaned	1000	1	1.916666667	0.00663512	1	0	1433.185814	4.5	
Sellers and Parker [7]	Cattle	O_1 Lombardy; O1 Swiss 1/66; O1 BFS 1860; O2 Brescia	316.227766 mice	BTY, Unweaned	1000	1	2.708333333	0.005270463	1	0	1138.419958	4.4	
											SUMMARY 4.7		4.5
Sellers et al. [6]	Cattle	O1 BFS 1860	398.1071706	BTY	1000	0.5	unknown	0.013270236	2	0	1433.185814	4.5	
Sellers et al. [6]	Cattle	O1 BFS 1860	251.1886432	BTY	1000	0.5	unknown	0.008372955	2	0	904.2791153	4.3	
Sellers et al. [6]	Cattle	O1 BFS 1860	316.227766	BTY	1000	0.5	unknown	0.010540926	2	0	1138.419958	4.4	
											SUMMARY 4.4		4.4
Alexandersen et al. [52]	Sheep	O UKG 34/2001	631	BTY	170	0.333333333	2	0.185588235	10	3	6013.058824	5.2	
Donaldson et al. [54]	Sheep	A5	15.84893192	BTY	1000	1	2	0.000264145	1	0	57.05615493	3.1	
Donaldson et al. [54]	Sheep	A22	11.22018454	BTY	1000	1	2	0.000187003	1	0	40.39266435	3.0	
Donaldson et al. [54]	Sheep	C Lebanon	10	BTY	1000	1	2	0.000166667	1	0	36	2.9	
Donaldson et al. [54]	Sheep	C Noville	31.6227766	BTY	1000	1	2	0.000527046	1	0	113.8419958	3.4	
Donaldson et al. [54]	Sheep	A5	11.22018454	BTY	1000	1	3	0.000187003	1	0	40.39266435	3.0	
Donaldson et al. [54]	Sheep	A22	10	BTY	1000	1	3	0.000166667	1	0	36	2.9	
Donaldson et al. [54]	Sheep	C Lebanon	0	BTY	1000	1	3	0	1	0	0	0.0	
Donaldson et al. [54]	Sheep	C Noville	19.95262315	BTY	1000	1	3	0.000332544	1	0	71.82944334	3.2	
											SUMMARY 2.7		3.0
Esteves et al. [55]	Sheep	O UKG 34/2001		BTY			1	0.020007305	1	10	11524.20751	5.4	
Sellers and Parker [7]	Sheep	O_1 Lombardy; O1 Swiss 1/66; O1 BFS 1860; O2 Brescia	251.1886432 mice	BTY, Unweaned	1000	1	1.708333333	0.004186477	1	0	904.2791153	4.3	
Sellers and Parker [7]	Sheep	O_1 Lombardy; O1 Swiss 1/66; O1 BFS 1860; O2 Brescia	70.79457844 mice	BTY, Unweaned	1000	1	2.708333333	0.00117991	1	0	254.8604824	3.8	
											SUMMARY 4.1		4.1

Study	Notes
Alexandersen and Donaldson [53]	(a) 2 (definite), 2 (maybe) infected animals during samplinig (using 3); (b) 3-5 ACH in loosebox (4 assumed); (c) data taken from Table 3; (d) dpi estimated from Fig 2 in Alexandersen JCP 2003; (e) pigs weight 25 kg
Alexandersen and Donaldson [53]	(a) 2 (definite), 2 (maybe) infected animals during samplinig (using 3); (b) 3-5 ACH in loosebox (4 assumed); (c) data taken from Table 3; (d) dpi estimated from Fig 2 in Alexandersen JCP 2003; (e) pigs weight 25 kg
Alexandersen et al. [50]	(a) 1 innoculation, 1 contact; (b) "peak" air concentrations and air exchange rate on p. 272
Sellers and Parker [7]	(a) value reported on per animal basis (8 pigs in loosebox); (b) data from Table 3
Sellers and Parker [7]	(a) value reported on per animal basis (8 pigs in loosebox); (b) data from Table 3
Donaldson et al. [56]	(a) 8 infected animals (early generalized lesions); (b) Litton sampler, ; (c) unclear on ACH (assumed blocked); (d) data from Table 1; (e) first day of sampling
Donaldson et al. [56]	(a) 8 infected animals (early generalized lesions); (b) Cyclone sample (actual sampling rate a 700 lpm, but reported values adjusted to 1000 lpm), ; (c) unclear on ACH (assumed blocked); (d) data from Table 1; (e) first day of sampling
Donaldson et al. [56]	(a) 8 infected animals (early generalized lesions); (b) Litton sampler, ; (c) unclear on ACH (assumed blocked); (d) data from Table 1; (e) first day of sampling
Donaldson et al. [56]	(a) 8 infected animals (early generalized lesions); (b) Cyclone sample (actual sampling rate a 700 lpm, but reported values adjusted to 1000 lpm), ; (c) unclear on ACH (assumed blocked); (d) data from Table 1; (e) first day of sampling
Donaldson et al. [56]	(a) 5 infected animals (generalized lesions); (b) Litton sampler, ; (c) unclear on ACH (assumed blocked); (d) data from Table 1; (e) second day of sampling
Donaldson et al. [56]	(a) 5 infected animals (generalized lesions); (b) Cyclone sample (actual sampling rate a 700 lpm, but reported values adjusted to 1000 lpm), ; (c) unclear on ACH (assumed blocked); (d) data from Table 1; (e) second day of sampling
Donaldson et al. [56]	(a) 5 infected animals (generalized lesions); (b) Litton sampler, ; (c) unclear on ACH (assumed blocked); (d) data from Table 1; (e) second day of sampling
Donaldson et al. [56]	(a) 5 infected animals (generalized lesions); (b) Cyclone sample (actual sampling rate a 700 lpm, but reported values adjusted to 1000 lpm), ; (c) unclear on ACH (assumed blocked); (d) data from Table 1; (e) second day of sampling
Donaldson et al. [54]	(a) data from Table 4; (b) average per animal (unclear on total number of animals sampled); (c) during sampling, no air exchange (Sellers JHC 1969); (d) 3x3x4 m loosebox
Donaldson et al. [54]	(a) data from Table 4; (b) average per animal (unclear on total number of animals sampled); (c) during sampling, no air exchange (Sellers JHC 1969); (d) 3x3x4 m loosebox
Donaldson et al. [54]	(a) data from Table 4; (b) average per animal (unclear on total number of animals sampled); (c) during sampling, no air exchange (Sellers JHC 1969); (d) 3x3x4 m loosebox
Donaldson et al. [54]	(a) data from Table 4; (b) average per animal (unclear on total number of animals sampled); (c) during sampling, no air exchange (Sellers JHC 1969); (d) 3x3x4 m loosebox
Donaldson et al. [54]	(a) data from Table 4; (b) average per animal (unclear on total number of animals sampled); (c) during sampling, no air exchange (Sellers JHC 1969); (d) 3x3x4 m loosebox
Donaldson et al. [54]	(a) data from Table 4; (b) average per animal (unclear on total number of animals sampled); (c) during sampling, no air exchange (Sellers JHC 1969); (d) 3x3x4 m loosebox
Donaldson et al. [54]	(a) data from Table 4; (b) average per animal (unclear on total number of animals sampled); (c) during sampling, no air exchange (Sellers JHC 1969); (d) 3x3x4 m loosebox
Donaldson et al. [54]	(a) data from Table 4; (b) average per animal (unclear on total number of animals sampled); (c) during sampling, no air exchange (Sellers JHC 1969); (d) 3x3x4 m loosebox
Gloster et al. [49]	(a) Table 3; (b) measurement by cyclone sampler; (c) airborne virus concentration converted from reported value (minus 1.2 to adjust for the ACH) by dividing by (cyclone flow rate * sampling duration) (see Gloster VJ 2006) and multiplying by the number of animals (this is consistent with the method described in Alexandersen JGV 2002)
Gloster et al. [49]	(a) Table 3; (b) measurement by cyclone sampler; (c) airborne virus concentration converted from reported value (minus 1.2 to adjust for the ACH) by dividing by (cyclone flow rate * sampling duration) (see Gloster VJ 2006) and multiplying by the number of animals (this is consistent with the method described in Alexandersen JGV 2002)
Gloster et al. [49]	(a) Table 3; (b) measurement by cyclone sampler; (c) airborne virus concentration converted from reported value (minus 1.2 to adjust for the ACH) by dividing by (cyclone flow rate * sampling duration) (see Gloster VJ 2006) and multiplying by the number of animals (this is consistent with the method described in Alexandersen JGV 2002)
Gloster et al. [49]	(a) Table 3; (b) measurement by cyclone sampler; (c) airborne virus concentration converted from reported value (minus 1.2 to adjust for the ACH) by dividing by (cyclone flow rate * sampling duration) (see Gloster VJ 2006) and multiplying by the number of animals (this is consistent with the method described in Alexandersen JGV 2002)
Gloster et al. [49]	(a) Table 3; (b) measurement by cyclone sampler; (c) airborne virus concentration converted from reported value (minus 1.2 to adjust for the ACH) by dividing by (cyclone flow rate * sampling duration) (see Gloster VJ 2006) and multiplying by the number of animals (this is consistent with the method described in Alexandersen JGV 2002)
Gloster et al. [49]	(a) Table 3; (b) measurement by cyclone sampler; (c) airborne virus concentration converted from reported value (minus 1.2 to adjust for the ACH) by dividing by (cyclone flow rate * sampling duration) (see Gloster VJ 2006) and multiplying by the number of animals (this is consistent with the method described in Alexandersen JGV 2002)
Gloster et al. [49]	(a) Table 3; (b) measurement by cyclone sampler; (c) airborne virus concentration converted from reported value (minus 1.2 to adjust for the ACH) by dividing by (cyclone flow rate * sampling duration) (see Gloster VJ 2006) and multiplying by the number of animals (this is consistent with the method described in Alexandersen JGV 2002)
Gloster et al. [49]	(a) Table 3; (b) measurement by cyclone sampler; (c) airborne virus concentration converted from reported value (minus 1.2 to adjust for the ACH) by dividing by (cyclone flow rate * sampling duration) (see Gloster VJ 2006) and multiplying by the number of animals (this is consistent with the method described in Alexandersen JGV 2002)
Gloster et al. [48]	(a) page 6, morning of day 2 dpi, 2nd study; (b) measurement scaled by cyclone sampler (reported value is average of Porton, May, and Cyclone measurements); (c) airborne virus concentration converted from reported value (minus 1 to adjust for the ACH, unclear if day at 18 ACH (- 1.2) or night at 9 ACH (-0.9)) by dividing by (cyclone flow rate * sampling duration) ar
Sellers et al. [6]	(a) Data from Table 1; (b) unknown time since infection (generalized lesions); (c) original difficult to read, may be 10x larger
Sellers et al. [6]	(a) Data from Table 1; (b) unknown time since infection (generalized lesions)
Sellers et al. [6]	(a) Data from Table 1; (b) unknown time since infection (generalized lesions)
Sellers et al. [6]	(a) Data from Table 1; (b) unknown time since infection (generalized lesions); (c) original difficult to read, may be 10x smaller
Sellers et al. [6]	(a) Data from Table 2; (b) unknown time since infection (generalized lesions)
Sellers et al. [6]	(a) Data from Table 2; (b) unknown time since infection (generalized lesions)
Sellers et al. [6]	(a) Data from Table 2; (b) unknown time since infection (generalized lesions)
Alexandersen et al. [52]	(a) direct innoculation; (b) excess nasal excretions; (c) 150 kg weight; (d) data from Table 2
Alexandersen et al. [52]	(a) direct innoculation; (b) excess nasal excretions; (c) 150 kg weight; (d) data from Table 2
Alexandersen et al. [52]	(a) direct innoculation; (b) mild generalized lesions; (c) 150 kg weight; (d) data from Table 2
Alexandersen et al. [52]	(a) direct innoculation; (b) mild generalized lesions; (c) 150 kg weight; (d) data from Table 2
Donaldson et al. [54]	(a) data from Table 2; (b) average per animal (unclear on total number of animals sampled); (c) during sampling, no air exchange (Sellers JHC 1969); (d) 3x3x4 m loosebox; (e) tongue innoculation
Donaldson et al. [54]	(a) data from Table 2; (b) average per animal (unclear on total number of animals sampled); (c) during sampling, no air exchange (Sellers JHC 1969); (d) 3x3x4 m loosebox; (e) tongue innoculation
Donaldson et al. [54]	(a) data from Table 2; (b) average per animal (unclear on total number of animals sampled); (c) during sampling, no air exchange (Sellers JHC 1969); (d) 3x3x4 m loosebox; (e) tongue innoculation
Donaldson et al. [54]	(a) data from Table 2; (b) average per animal (unclear on total number of animals sampled); (c) during sampling, no air exchange (Sellers JHC 1969); (d) 3x3x4 m loosebox; (e) tongue innoculation
Donaldson et al. [54]	(a) data from Table 2; (b) average per animal (unclear on total number of animals sampled); (c) during sampling, no air exchange (Sellers JHC 1969); (d) 3x3x4 m loosebox; (e) tongue innoculation
Donaldson et al. [54]	(a) data from Table 2; (b) average per animal (unclear on total number of animals sampled); (c) during sampling, no air exchange (Sellers JHC 1969); (d) 3x3x4 m loosebox; (e) tongue innoculation
Donaldson et al. [54]	(a) data from Table 2; (b) average per animal (unclear on total number of animals sampled); (c) during sampling, no air exchange (Sellers JHC 1969); (d) 3x3x4 m loosebox; (e) intramuscular innoculation
Donaldson et al. [54]	(a) data from Table 2; (b) average per animal (unclear on total number of animals sampled); (c) during sampling, no air exchange (Sellers JHC 1969); (d) 3x3x4 m loosebox; (e) intramuscular innoculation
Donaldson et al. [54]	(a) data from Table 2; (b) average per animal (unclear on total number of animals sampled); (c) during sampling, no air exchange (Sellers JHC 1969); (d) 3x3x4 m loosebox; (e) pig exposure - significant airborne levels at 7 dpi (similar to other measurements)
Sellers and Parker [7]	(a) value reported on per animal basis (2 cattle in loosebox); (b) data from Table 1
Sellers and Parker [7]	(a) value reported on per animal basis (2 cattle in loosebox); (b) data from Table 1
Sellers and Parker [7]	(a) value reported on per animal basis (2 cattle in loosebox); (b) data from Table 1
Sellers et al. [6]	(a) Data from Table 4; (b) unknown time since infection (generalized lesions)
Sellers et al. [6]	(a) Data from Table 4; (b) unknown time since infection (generalized lesions)
Sellers et al. [6]	(a) Data from Table 4; (b) unknown time since infection (generalized lesions); (c) cattle moved in 45 min prior to sampling
Alexandersen et al. [52]	(a) unclear if source from innoculation (6) or direct contact (4) sheep (cabinet studies suggest direct contact); (b) sheep sheared; (c) 30 kg weight; (d) clinical signs: 1-2 dpi innoculation; 2-6 days direct contact; (e) data from Table 1
Donaldson et al. [54]	(a) data from Table 3; (b) average per animal (unclear on total number of animals sampled); (c) during sampling, no air exchange (Sellers JHC 1969); (d) 3x3x4 m loosebox
Donaldson et al. [54]	(a) data from Table 3; (b) average per animal (unclear on total number of animals sampled); (c) during sampling, no air exchange (Sellers JHC 1969); (d) 3x3x4 m loosebox
Donaldson et al. [54]	(a) data from Table 3; (b) average per animal (unclear on total number of animals sampled); (c) during sampling, no air exchange (Sellers JHC 1969); (d) 3x3x4 m loosebox
Donaldson et al. [54]	(a) data from Table 3; (b) average per animal (unclear on total number of animals sampled); (c) during sampling, no air exchange (Sellers JHC 1969); (d) 3x3x4 m loosebox
Donaldson et al. [54]	(a) data from Table 3; (b) average per animal (unclear on total number of animals sampled); (c) during sampling, no air exchange (Sellers JHC 1969); (d) 3x3x4 m loosebox
Donaldson et al. [54]	(a) data from Table 3; (b) average per animal (unclear on total number of animals sampled); (c) during sampling, no air exchange (Sellers JHC 1969); (d) 3x3x4 m loosebox
Donaldson et al. [54]	(a) data from Table 3; (b) average per animal (unclear on total number of animals sampled); (c) during sampling, no air exchange (Sellers JHC 1969); (d) 3x3x4 m loosebox
Donaldson et al. [54]	(a) data from Table 3; (b) average per animal (unclear on total number of animals sampled); (c) during sampling, no air exchange (Sellers JHC 1969); (d) 3x3x4 m loosebox
Esteves et al. [55]	(a) Table 1; (b) measurement normalized by cyclone sampler as reported in Alexandersen JGV 2002; (c) airborne virus concentration converted from reported method B value (minus 1.0 to adjust for the ACH) by dividing by (cyclone flow rate * 60 min * 24 hr) and multiplying by the number of animals (this is consistent with the method described in Alexandersen JGV 20(
Sellers and Parker [7]	(a) value reported on per animal basis (8 sheep in loosebox); (b) data from Table 2; (c) highest emissions at 17 hrs pi
Sellers and Parker [7]	(a) value reported on per animal basis (8 sheep in loosebox); (b) data from Table 2; (c) highest emissions at 17 hrs pi

1) **Room size** 36000 L

2) **Loosebox Loss Rates**

Reference	Virus	Animal	First Sample (TCID50)	Second Sample (TCID50)	Ratio of Second to First Sample	First Sample Sampling Duration (min)	Second Sample Sample Start Time (min from animal removal)	Second Sample Sample Stop Time (min from animal removal)	Fitted Loss Rate (1/min)	Predicted Second Sample (TCID50)	Difference Between Measured and Predicted Second Sample (%)	Notes
Sellers and Herniman [58]	O1 BFS 1860; A Pando; C Noville	swine	25118.86432	15848.93192	0.630957	25	5	30	0.028	15704.59071	0.910731515	(a) Table 2
Sellers and Herniman [58]	O1 BFS 1860; A Pando; C Noville	swine	50118.72336	6309.573445	0.125893	25	5	30	0.148	6303.011612	0.103998039	(a) Table 2
Sellers and Herniman [58]	O1 BFS 1860; A Pando; C Noville	swine	199526.2315	25118.86432	0.125893	25	5	30	0.148	25092.74119	0.103998039	(a) Table 2
Sellers and Herniman [58]	O1 BFS 1860; A Pando; C Noville	swine	199526.2315	19952.62315	0.1	25	5	30	0.17	19779.77172	0.866309322	(a) Table 2
Sellers and Herniman [58]	O1 BFS 1860; A Pando; C Noville	swine	1258925.412	12589.25412	0.01	25	5	30	0.442	12497.98552	0.724972231	(a) Table 2
Sellers and Herniman [58]	O1 BFS 1860; A Pando; C Noville	swine	5011872.336	199526.2315	0.039811	25	5	30	0.265	200815.5471	-0.646188541	(a) Table 2
Sellers and Herniman [58]	O1 BFS 1860; A Pando; C Noville	swine	199526.2315	19952.62315	0.1	25	5	30	0.17	19779.77172	0.866309322	(a) Table 2
Sellers and Herniman [58]	O1 BFS 1860; A Pando; C Noville	swine	316227.766	50118.72336	0.158489	25	5	30	0.127	50575.25872	-0.910907803	(a) Table 2
Sellers and Herniman [58]	O1 BFS 1860; A Pando; C Noville	swine	12589254.12	199526.2315	0.015849	25	5	30	0.38	198191.2013	0.669100075	(a) Table 2
Sellers and Herniman [58]	O1 BFS 1860; A Pando; C Noville	swine	50118.72336	501.1872336	0.01	25	60	85	0.065	501.373606	-0.037186176	(a) Table 2
Sellers and Herniman [58]	O1 BFS 1860; A Pando; C Noville	swine	1258925.412	1258.925412	0.001	25	60	85	0.099	1226.122223	2.605649893	(a) Table 2
Sellers and Herniman [58]	O1 BFS 1860; A Pando; C Noville	swine	5011872.336	7943.282347	0.001585	25	60	85	0.092	7853.879079	1.125520458	(a) Table 2
Sellers et al. [6]	O1 BFS 1860	swine	316227.766	10000	0.031623	30	30	60	0.082	10044.19343	-0.44193432	(a) Table 2, exp 5
Sellers et al. [6]	C Noville	swine	3981071.706	158489.3192	0.039811	30	30	60	0.076	160329.1905	-1.160880307	(a) Table 2, exp 6
Sellers et al. [6]	O1 BFS 1860	swine	3981071.706	12589.25412	0.003162	30	30	60	0.143	12543.71693	0.36171475	(a) Table 2, exp 7; (b) last digit hard to read
Sellers et al. [6]	unknown	swine	630957.3445	25118.86432	0.039811	30	60	90	0.044	24998.41301	0.479525301	(a) Table 3
Sellers et al. [6]	unknown	swine	630957.3445	1000	0.001585	30	240	270	0.025	1100.282393	-10.0282393	(a) Table 3
Sellers et al. [6]	unknown	swine	630957.3445	158.4893192	0.000251	30	1440	1470	0.0057	158.0184214	0.29711643	(a) Table 3
Sellers et al. [6]	O1 BFS 1860	cattle	398.1071706	251.1886432	0.630957	30	30	60	0.01	254.7973271	-1.43664294	(a) Table 4, exp 1; (b) excluded from analysis due to low measured values
Sellers et al. [6]	O1 BFS 1860	cattle	251.1886432	199.5262315	0.794328	30	30	60	0.005	200.7663005	-0.621506746	(a) Table 4, exp 2; (b) excluded from analysis due to low measured values
Sellers et al. [6]	O1 BFS 1860	cattle	316.227766	158.4893192	0.501187	30	30	60	0.016	155.406516	1.945117345	(a) Table 4, exp 3; (b) excluded from analysis due to low measured values

Loss rate used in this study = 0.1 1/min
6 1/hr
144 1/day

(a) loss rate value chosen to correspond to the short term (30 min) loss rates observed in the swine data